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NON-MENINGOCOCCAL PURULENT MENINGITIS IN INFANCY AND CHILDHOOD

A STUDY OF 52 CASES *

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The diagnosis of meningitis until relatively recently carried with it an extremely gloomy prognosis, causing despair to both the parents and the paediatrician. The introduction of the sulphonamides and antibiotics has completely changed the outlook for patients suffering from purulent meningitis. It has been stated that the mortality rate should not exceed 10% in cases of meningococcal and 'influenzal' meningitis and 20% in pneumococcal meningitis.[1]

This paper deals with a study of 52 cases of purulent meningitis in infancy and childhood treated at Groote Schuur Hospital in the 2 years July 1955 to June 1957. The series comprises 22 cases caused by the pneumococcus, 9 by *Haemophilus influenzae* and 10 by *Haemophilus para-influenzae*, and 11 cases where a causal organism was not identified with certainty (of which the cerebrospinal fluid (C.S.F.) obtained on admission was purulent in every case and in 6 cases showed organisms in stained preparations, but in no case was the organism isolated on culture). Meningococcal infections are not treated at Groote Schuur Hospital but at the City Hospital for Infectious Diseases, Cape Town, and thus do not appear in the series. A few rare forms of meningitis seen during this period are excluded.

Of the 52 patients 36 were aged 7 months and less, 11 were between 7 months and 1 year, and 5 were older than a year. Only 3 were Europeans. A large number were malnourished, many had rickets and most had some degree of anaemia. Several had severe diarrhoea complicating their illness and required parenteral administration of fluid.

The objects of the study were:

1. To test a simple therapeutic regime for pyogenic meningitis.
2. To determine the speed with which the CSF becomes sterile.
3. To correlate the timing of CSF changes with immediate prognosis during treatment.
4. To estimate the significance of continued pyrexia.
5. To assess the prognostic significance of the clinical picture on admission.

* A paper presented at the South African Medical Congress, Durban, September 1957.

SCHEME OF TREATMENT

In 22 cases the patients received no intrathecal treatment. Because of the delay in arranging for admission to our overcrowded wards, all the other children were given an intrathecal injection immediately after the withdrawal of CSF for diagnostic purposes—15 cases received 10,000 units of penicillin, 12 cases 200 micrograms of chloramphenicol, and 2 cases 10,000 units of penicillin plus 200 micrograms of chloramphenicol. Further treatment was determined by the apparent aetiology as judged by the smear made from the first specimen of CSF. When the result of the culture became available the treatment was modified or altered if the initial assessment was shown to be at fault.

Pneumococcal Meningitis. Tetracycline has a wide range of anti-bacterial activity and is known to cross the blood-brain barrier well.[2-5] It was decided to treat our cases of pneumococcal meningitis with this antibiotic. After a loading dose of tetracycline hydrochloride (Achromycin, Lederle), 10 mg./lb. by intramuscular injection, it was continued in a dosage of 10 mg./lb./day divided into 3 eight-hourly intramuscular injections. Sulphadiazine was given in addition, 2 gr./lb./day orally, or by stomach tube in comatose patients. In 6 cases, only tetracycline was given.

Haemophilus influenzae and para-influenzae. In the influenzal cases, after a loading dose of chloramphenicol, 50 mg./lb. by intramuscular injection, treatment consisted of chloramphenicol 50 mg./lb./day in 8-hourly doses by intramuscular injection. Oral sulphadiazine was also given, as in the pneumococcal cases.

Cases where No Organism was Identified. Of these cases, 7 received chloramphenicol, tetracycline and sulphadiazine, 2 received tetracycline and sulphadiazine, 1 received chloramphenicol and sulphadiazine, and 1 received tetracycline only.

This variation in treatment was due to the uncertainty of the aetiology and occasionally to misinterpretation of instructions. Treatment was often decided by a knowledge of which drugs the patient had received before admission. Some patients were doing so well on the provisional treatment started before receipt of the culture report that it was not changed, even though the suspected type of infection was not confirmed.

Treatment was continued for 10 days in all the groups. Sedatives were used liberally. As the condition of the patients improved the drugs were given orally.

RESULTS OF TREATMENT

Table I shows the results of treatment. There were 22 cases of pneumococcal meningitis with 16 recoveries, i.e. a recovery rate of 73%. Of the 6 children who received tetracycline but no sulphadiazine, 4 recovered. There were 19 cases of haemophilus meningitis with 14 recoveries, i.e. a recovery rate of 74%. In the non-identified group 10

TABLE I. RESULTS OF TREATMENT

	Cases	*Recoveries*	%	*Deaths*
Pneumococcus ..	22	16	73	6
H. influenzae ..	9	7	74	2
H. para-influenzae ..	10	7		3
Not identified ..	11	10	91	1
	52	40	77	12 (23%)

survived out of 11 cases seen, i.e. a recovery rate of 91%. The child who died had received a combination of all three drugs. In the last-mentioned group more than half had had some form of treatment prescribed before admission to hospital and it is possible that some of these infections were already partially controlled by this treatment.

It is generally accepted that meningitis carries a graver prognosis in the early months of life than in later childhood. Most of our cases were 7 months old and younger; 36 fell into this group (about 70%); 11 were between 7 months and 1 year; 5 were over one year of age, the oldest being 5 years.

The results of treatment in the age-group 7 months and under are shown in Table II. There were 16 pneumococcal

TABLE II. RESULTS OF TREATMENT IN THE AGE-GROUP 7 MONTHS AND UNDER

	Cases	*Recoveries*	*Deaths*
Pneumococcus	16	10	6
H. influenzae	5	4	1
H. para-influenzae	8	5	3
Not identified	7	7	—
	36	26	10

cases with 6 deaths. There were 5 influenzal cases with 1 death, and 8 para-influenzal cases with 3 deaths. No deaths occurred in the 7 children of the unidentified infections. Thus, out of a total of 12 deaths in the whole series, 10 occurred in this age-group; that is to say, 83% of the deaths occurred in babies less than 8 months old.

Time of Death. Of the 'pneumococcal' deaths 3 occurred within 24 hours of admission, one of them within the first hour; 2 died on the 6th day and 1 on the 16th. Of the 'haemophilus' deaths 2 occurred on the 3rd day, 1 on the 7th, 1 on the 17th and 1 on the 28th. The child in the non-identified group died on the 10th day.

Autopsies were performed in 7 cases. The residual meningeal exudate was cultured in 2 cases, but the causal organism could no longer be isolated. In one case death appeared to be due to a terminal staphylococcal septicaemia. One patient was found to have a cerebral abscess in addition to meningitis. Subdural effusions were not found.

Neurological Sequelae. These are shown in Table III. Among the pneumococcal cases there were 2 mentally retarded and spastic children. One was a baby of 2 months, and the other was a child of 14 months who had been retarded and epileptic before his illness. A 7-month-old

TABLE III. RESULTS IN 39 SURVIVORS

	Pneumo-coccus	*Haemo-philus*	*Not identified*
Mentally retarded and spastic ..	2	—	1
Spastic hemiparesis or hemiplegia	1	1	—
	3	1	1

infant had a spastic hemiparesis which was rapidly improving when seen as an out-patient two weeks after discharge. Among the haemophilus group one 10-month-old infant was left with a spastic hemiplegia. Among the non-identified group an 11-month-old was left spastic and retarded.

CLINICAL PATHOLOGY

Bacteriology of the Cerebrospinal Fluid

Preparations of the initial specimens of CSF were stained with Gram's stain. The causal organism was found in all the cases of pneumococcal and *H. influenzae* infection and confirmed by culture. In the 10 *H. para-influenzae* group the organism was found in 7 of the initial smears; in 2 no organism was seen and in 1 the appearance of the organism was equivocal. Culture of these 10, however, demonstrated the nature of the infection.

In the group where no organism was isolated on culture, Gram-negative bacilli had been seen on the initial smear in 2 cases and Gram-positive diplococci in 4.

Table IV shows the results of CSF culture after 48 hours' treatment. In the pneumococcal group 11 of the 12 fluids

TABLE IV. CSF CULTURE AFTER 48 HOURS' TREATMENT (32 CASES)

	Negative			*Positive*	
Pneumococcal	11	14		1	
	*3				
H. influenzae	4		26	3	6
H. para-influenzae	6	12		2	
	*2	8			

* After 24 hours' treatment.

tested were sterile. The 3 most recent cases were checked at 24 hours and found to be sterile. The *H. influenzae* group showed 4 sterile out of the 7 cultured at 48 hours, and in the *H. para-influenzae* cases 6 of the 8 tested were sterile. Again, the CSF of the 2 most recent cases of para-influenzae infection was cultured at 24 hours and showed no growth.

Of the 6 children who had positive CSF cultures 48 hours after the commencement of treatment 3 died and 1 had a residual hemiplegia. Of the 14 patients in the pneumococcal group with sterile fluids at 48 hours, 2 died and 2 are mentally retarded. The 4 in the influenzal group all recovered completely but in the para-influenzal group, of 8 children with sterile 48 hour cultures, 2 died. Thus, though treatmen- produced rapid sterilization of the CSF, there was a cont

siderable mortality and morbidity. There was no recurrence of infection in any case of the series.

Other Changes in the CSF. In all but one of the 52 patients there was initially a polymorph preponderance on the CSF smear. The exception was a case of *H. para-influenzae* meningitis which showed a mononuclear picture. Pandy's test for increased globulin was positive in 38 cases out of 39 tested. It was negative in 1 case of pneumococcal meningitis. The sugar content of the CSF showed considerable variation on qualitative testing (Table V). In 38 cases, sugar was absent in 22, diminished in 12 and normal in 4.

TABLE V. QUALITATIVE SUGAR ESTIMATION

	Cases	*Absent*	*Diminished*	*Normal*
Pneumococcus ..	12	7	3	2
H. influenzae ..	8	6	2	0
H. para-influenzae ..	9	4	4	1
Not identified ..	9	5	3	1
	38	22	12	4

At the commencement of the study we were uncertain whether treatment should be continued until the CSF was completely normal. In 3 cases abnormalities persisted into the 3rd week and in 2 others beyond the 4th week. These 5 children all became normal despite the fact that treatment had not been prolonged beyond the standard time. In these cases, however, the cells persisting in the CSF were mononuclears and the sugar had returned to normal or nearly so. It appears that if the CSF is sterile a raised cell count does not necessitate prolongation of therapy so long as the sugar is returning to normal and the cellular response is not polymorphonuclear.

PROGNOSIS

The Significance of Continued Pyrexia

In most cases the temperature settled after the 4th day of treatment, but in a fair number it persisted for a week. Subdural taps were done on 11 of these children and were found to be positive in 5. Where subdural effusions were present, there were other signs in addition to pyrexia, e.g. continuing convulsions, increasing spasticity, deepening coma, and full fontanelle. It would appear that when persistent pyrexia is the only untoward sign the prognosis is not likely to be adversely affected.

The Prognostic Significance of the Clinical Picture on Admission

Table VI shows the course taken by the cases in relation to their state on admission.

Ten children were comatose on admission. Of these 7 died, 2 recovered completely and 1 who had been retarded before his attack of meningitis remained so. Four of these comatose children were spastic and, of these, 3 died and the other was the retarded child. One comatose child had one spastic limb and recovered completely. Among the 5 comatose children who showed no evidence of spasticity 4 died and 1 recovered completely. Thus 70% *of the children comatose on admission died.*

Twelve children were stuporose on admission. Of these, 3 died, and of those who recovered 1 was retarded, 1 had a hemiplegia and 1 a hemiparesis, and 6 recovered completely. Three of these stuperose children were spastic and, of the three, 1 died and 1 was hemiplegic and 1 hemiparetic. Two of the stuporose children had spasticity in a single limb and of these 1 died and 1 is normal. Of the 7 stuporose children without signs of spasticity 1 died, 5 are normal and 1 was left with a hemiparesis. Thus 25% *of the children stuporose on admission died.*

TABLE VI. ADMISSION STATE AND PROGNOSIS

	Cases	*Deaths*	*Sequelae*	*Normal*	
Coma					
+ generalized spasticity ..	4	3	1	—	
+ localized spasticity ..	1	—	—	1	
without spasticity ..	5	4	—	1	
Total ..	10	7	1	2	
Stupor					25%*
+ generalized spasticity ..	3	1	2	—	
+ localized spasticity ..	2	1	—	1	
without spasticity ..	7	1	1	5	
Total ..	12	3	3	6	
Conscious					7%
+ spasticity (hemiplegia) ..	2	1	1	—	
without spasticity ..	28	1	—	27	
Total ..	30	2	1	27	

* Mortality.

Thirty children were conscious on admission. Of these 2 died. Two of the conscious children had a spastic hemiplegia on admission. One died and autopsy revealed a cerebral abscess. The other was left spastic and retarded. Thus 7% *of the children conscious on admission died.*

These findings suggest that coma is a grave prognostic sign. Stupor and spasticity also adversely affect the outcome. No child showing generalized spasticity on admission recovered completely.

Chest Radiography

Radiographs of the chest were taken in 48 cases. The results are shown in Table VII. In 20 cases of pneumococcal meningitis bronchopneumonia was found to be present in 7, lobar pneumonia in 1, and pulmonary tuberculosis in 1. In 15 cases of haemophilus infection 3 children showed bronchopneumonia and 1 empyema. Three cases of bronchopneumonia were found in the 13 belonging to the unidentified group. Thus pneumonia occurred most frequently in the cases of pneumococcal meningitis, but no correlation could be found between this finding and the course or result of the meningitis.

TABLE VII. RESULTS OF X-RAY EXAMINATION OF THE CHEST

	Cases	*Broncho-pneumonia*	*Lobar pneumonia*	*Tuber-culosis*	*Empyema*
Pneumococcus	20	7	1	1	
Haemophilus	17	3			1
Unidentified	11	3			
	48	13	1	1	1

COMMENT

While this series is not large enough to permit of many definite conclusions several interesting facts emerge.

Out of the 22 cases of pneumococcal meningitis 16 sur-

vived. If the cases dying within 24 hours of admission are excluded, there were 16 survivals out of 19 cases, a recovery rate of 83%. We may conclude that tetracycline plus sulphadiazine is an effective combination. The fact that there were 4 survivors out of the 6 cases treated with tetracycline only, further suggests that tetracycline is an effective drug for the treatment of pneumococcal meningitis.

Out of the 19 cases of haemophilus infection 14 survived. It is surprising that this group did not do better than the pneumococcal group. It may be that the onset of haemophilus meningitis is more insidious and that our patients did not come to hospital until the disease was well advanced.

Out of the 11 in the unidentified group 10 survived. This suggests that this group carries a very good prognosis; but it is difficult to deduce which is the best drug or combination of drugs to use in treating them.

The results are encouraging which were obtained with this simple regime of one intrathecal injection at the time of the discovery of a purulent CSF and systemic treatment only thereafter. The virtual exclusion of intrathecal treatment makes it a method of treatment applicable to country practice. An over-all recovery rate of 77% in cases of purulent meningitides, in patients of non-European race and with indefinite but frequently prolonged illness before the institution of treatment, may not be the best obtainable, but under such circumstances and in such subjects is at least an improvement on former results.

In 26 of the 32 CSF cultures checked 24-48 hours after the start of treatment, there was no growth. Of the 7 deaths in these 32 children, 4 were in those with negative 48-hour cultures, and such negative culture is therefore not a reliable prognostic point. The fact that in the 39 survivors there were no relapses of the infection indicates the adequacy of the anti-infective therapy.

Coma is the gravest single prognostic sign. The occurrence of spasticity also adversely affects the prognosis. More intensive treatment or some adjuvant to the current anti-infective treatment may be required. The use of cortisone merits consideration and closer attention to electrolyte disturbance and its importance in the production of cerebral oedema may be beneficial. The finding of 5 survivors with serious sequelae, though this is not a high figure—13% of the survivors—seems to point in the same direction, namely, concentration on the non-bacterial aspect of meningitis.

SUMMARY

1. A simple scheme for the treatment of pyogenic meningitis is described. This consists of an initial intrathecal injection followed by systemic treatment only.

2. The results of this regime in 52 cases are described. The general recovery rate was 77%.

3. Effective sterilization of the CSF was shown in 26 of 32 tests made within 48 hours of starting treatment.

4. Persistence of some fever for a week, or of a raised CSF cell count for as long as 4 weeks, was not of bad prognostic significance.

5. Of the 39 recoveries 5 were associated with serious sequelae.

6. Coma at the time of admission was associated with a 70% mortality and stupor with a 25% mortality.

7. No patient showing generalized spasticity on admission recovered completely.

8. It is suggested that further improvement in mortality figures will be dependent on measures other than the antibacterial treatment.

It is a pleasure to acknowledge the permission of the hospital Superintendent to publish these figures and the help and encouragement of the Professor of Child Health in preparing this paper.

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EDITORIAL

SURGICAL FATALITIES

The rate of mortality in patients undergoing certain operations in teaching hospitals in the UK has recently been compared with another group of patients undergoing similar operations in non-teaching hospitals.[1] The operations considered were appendicitis with peritonitis, perforated peptic ulcer, and hyperplasia of the prostate. All 3 groups show that in a large series of figures and taken over some time, the mortality among the cases in the non-teaching hospitals was substantially greater than in the teaching hospitals. In the group of appendicitis with peritonitis 3·4% died in the teaching as opposed to 6·8% in the non-teaching hospitals. In the group of perforated peptic ulcer the relative figures were 7·6% and 10·6%, and in cases of operation for hyperplasia of the prostate the mortality was 7·1% in the teaching as compared with 10·8% in the non-teaching hospitals.

These statistics are revealing; their publication will stimulate many opinions on the reason for the disparity and doubtless many suggestions will be made how the standard of surgery in the non-teaching hospitals can be brought closer to that obtaining in the teaching hospitals. It seems from the figures that the patient who dislikes going into a teaching hospital and who persistently refuses to be examined by students is displaying not only foolishness but sheer foolhardiness.

Surgery is now a mature science, although informed opinion will not conclude that we have reached the limits of surgical progress. The maturity of a medical discipline is measured not by the high percentage of its successes, but by the fewness of its failures. As in modern air travel, no matter how vast the number of successful flights an air line has to its credit, the report of a few crashes is most damaging to its reputation. That the safety of surgery has reached a stage where it can be compared with that of modern air travel should be a matter for general satisfaction. Where one surgeon, for example, reports with pride a recovery rate of 97%, another one with a recovery rate of 98% may well point out that his mortality figures are less by 50% than those of his colleague, although the difference between 97 and 98% does not look very great; it is on this fatality rate that the danger of operations must be assessed and judged. It is no longer a surgical miracle that a patient survives; on the contrary it is a matter for record when a

VAN DIE REDAKSIE

CHIRURGIESE STERFTES

Die sterftesyfer onder pasiënte wat sekere operasies in opleidingshospitale in die Verenigde Koninkryk ondergaan het, is onlangs vergelyk met dié van 'n ander groep wat soortgelyke operasies in gewone hospitale ondergaan het.[1] Die operasies wat in aanmerking geneem was, was vir blindedermontsteking met buikvliesontsteking, deurborende maagseer, en hiperplasie van die voorstanderklier. In 'n groot reeks gegewens wat oor 'n aansienlike tydperk aangeteken was, is bevind dat die sterftesyfer by al 3 groepe aansienlik groter was in die gewone hospitale as in die opleidingshospitale. In die groep blindedermontsteking met buikvliesontsteking het 3·4% pasiënte in die opleidingshospitale gesterf en 6·8% in die gewone hospitale. In die groep deurborende maagsere was die syfer 7·6% en 10·6% onderskeidelik, en by die gevalle van operasie vir hiperplasie van die voorstanderklier was die sterftesyfer 7·1% in die opleidingshospitale en 10·8% in die gewone hospitale.

Hierdie statistieke is veelbetekenend; hulle publikasie sal uiteenlopende menings oor die rede vir die verskil uitlok en daar sal ongetwyfeld baie voorstelle aan die hand gedoen word oor hoe die gehalte van die snykunde in die gewone hospitale verbeter kan word om gunstig te vergelyk met dié wat in die opleidingshospitale heers. Uit die gegewens blyk dit dat die pasiënt wat nie daarvan hou om in 'n opleidingshospitaal behandel te word nie en wat altyd weier om deur mediese studente ondersoek te word, hom nie alleen aan dwaasheid skuldig maak nie maar ook aan louter roekeloosheid.

Die snykunde is vandag 'n volwasse wetenskap, hoewel deskundiges nie sal beweer dat ons die perke van chirurgiese vooruitgang bereik het nie. Die volwassenheid van 'n mediese dissipline word gemeet aan die skaarsheid van sy mislukkings eerder as aan die hoë persentasie van sy suksesse. Net soos by die moderne lugvaart: 'n maatskappy se reputasie kan oneindig veel skade ly deur die verslag van 'n paar rampe, nieteenstaande die ontelbare suksesvolle vlugte waarop hy kan roem. Dit behoort rede vir algemene tevredenheid te wees dat die veiligheid van die snykunde vandag die stadium bereik het waar dit vergelyk kan word met moderne lugvaart. Waar 'n chirurg byvoorbeeld met trots kan spog met 'n herstelsyfer van 97%, kan 'n ander een met 'n herstelsyfer van 98% daarop aanspraak maak dat sy sterftesyfer 50% minder as dié van sy kollega s'n is, hoewel die verskil tussen 97% en 98% nie baie groot lyk nie; dit is dan ook volgens hierdie sterftesyfer wat die gevaar van operasie bereken en beoordeel moet word. Dit is vandag nie 'n chirurgiese wonderwerk as 'n pasiënt die operasie oorleef nie; dit is eerder iets om van te praat as hy sterf. Chirurge, algemene praktisyns en die publiek is daarop geregtig om te weet dat die uitdrukking ‚aan hulle goeie

fatality occurs. Surgeons, general practitioners and the general public are entitled to know that the expression 'By their good deeds shall ye know them' is no longer applicable to modern surgical figures; on the contrary, by their bad results shall ye know them.

In a country such as England where the general standard of medical competence has always been very high and where surgical ability parallels technical competence in other matters, it is surprising to find these relatively high mortality figures in the non-teaching hospital. There is no doubt that in a teaching hospital there is less room for the self-opinionated, conceited surgeon. More self-criticism and less pride help to keep the figures of mortality low, but the greater factor in reducing the death rate is effective pre- and post-operative treatment, and a healthy critical spirit in the wards, the theatre and the autopsy room. In modern surgery the actual operation itself is only a phase, and that not always the most important one, in what may be a long course of therapy. In spite of their better figures the operators in teaching hospitals are often only recently qualified junior men who are learning their trade; the very nature of learning implies that this must be so. In the non-teaching hospitals the non-supervised, often senior, but often also occasional operator may be held responsible for much of the unfavourable results, but other factors may play a great part. It is the painstaking pre-operative care and meticulous post-operative attention which brings success and makes the statistics we expect and hope to achieve.

Perhaps linked with this matter is another British report, made by the Select Committee on Estimates to the House of Commons on the Running Costs of Hospitals.[2] The average London teaching hospital has an in-patient cost of £27 per week as compared with £18 per week for the average acute 300-900 bed non-teaching hospital. The Committee recommends that until the standards of non-teaching hospitals reach a significantly higher level the allocation of development and improvement money to teaching hospitals should continue to be strictly limited. It thus appears that the first step in Great Britain is going to be a raising of the standards of the non-teaching hospitals before the teaching hospitals are to be allowed to spurt still further ahead.

Doubtless the matter received much thought before this important decision was reached. We are not in a position to offer advice or opinions on this subject to our colleagues in Great Britain. A country whose medical journals are prepared to publish these damaging figures is certainly capable of finding out the proper means of correcting the trouble.

For us in South Africa, the publication of the British statistics should lead to an early assessment of the state of affairs in our non-teaching hospitals. While we believe that our teaching hospitals can stand comparison with any in the world for the excellent pre- and post-operative treatment of their patients—various reports on long series of operations have tended to confirm this opinion—a survey of results in non-teaching hospitals should be undertaken in the near future to afford a reliable assessment of results and incidentally to prevent undue pessimism on the one hand and an undue state of satisfaction on the other.

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2. Article (1957): *The Running Cost of Hospitals*. *Ibid.*, 2, 739.

dade sal julle hulle ken' nie meer van toepassing op chirurgiese statistieke is nie; inteendeel, aan hulle mislukkings sal julle hulle ken.

In 'n land soos Engeland waar die algemene standaard van geneeskunde nog altyd baie hoog was en waar snykundige bedrewenheid kers kan vashou by tegniese deskundigheid op ander gebiede, is dit verbasend dat sulke betreklik hoë sterftesyfers in die gewone hospitale aangetref word. Daar is seer sekerlik nie plek vir die eiewyse, verwaande chirurg in 'n opleidingshospitaal nie. Meer selfkritiek en minder hoogmoed help om die sterftesyfer laag te hou, maar die grootste faktor by die beperking van die sterftesyfer is doeltreffende voor- en naoperatiewe behandeling, en 'n gesonde kritiese gees in die saal, die teater en die lykskouingskamer. In die moderne snykunde is die operasie self slegs 'n deel van 'n moontlik baie lang behandelingskursus, en dan ook nie altyd dié belangrikste nie. Nieteenstaande hul gunstiger statistieke is die chirurge in opleidingshospitale dikwels jong mans wat so pas gekwalifiseer het en wat nog hulle vak leer; dit volg uit die aard van die opleiding. In die gewone hospitaal kan die chirurg wat sonder toesig werk, en wat dikwels 'n senior man is, maar dikwels ook een is wat nie so gereeld opereer nie, verantwoordelik gehou word vir baie van die ongunstige resultate, maar daar is ander faktore wat ook 'n belangrike rol speel. Dit is die noulettende voor-operatiewe sorg en sorgvuldige na-operatiewe toesig wat die operasie laat slaag en die statistieke wat ons verwag en hoop om te behaal, moontlik maak.

Moontlik staan 'n ander Britse verslag deur die *Select Committee on Estimates* aan die Britse Laerhuis insake die lopende uitgawes van hospitale[2] in verband hiermee. Die gemiddelde Londense opleidingshospitaal se uitgawe vir binne-pasiënte beloop £27 per week, teenoor £18 per week vir die gemiddelde gewone hospitaal vir akute gevalle met 300-900 beddens. Hierdie Komitee beveel aan dat tot tyd en wyl die standaard van gewone hospitale aansienlik verbeter, die toekenning aan opleidingshospitale van fondse vir ontwikkeling en verbeterings nog altyd streng beperk moet word. Dit blyk dus dat die owerhede in Groot-Brittanje hulle eerstens daarop gaan toelê om die gehalte van die gewone hospitale op hoogte te bring voordat die opleidingshospitale toegelaat gaan word om verder vooruit te skiet.

Die saak het ongetwyfeld baie aandag geniet voordat hierdie belangrike besluit geneem is. Dit betaam ons nie om oor hierdie onderwerp raad te gee of menings uit te spreek aan ons kollegas in Groot-Brittanje nie. Die land wie se mediese tydskrifte bereid is om sulke ongunstige gegewens te publiseer, is seer sekerlik in staat om self te besluit hoe die moeilikheid ten beste opgelos kan word.

Vir ons in Suid-Afrika behoort die publikasie van hierdie gegewens 'n aansporing te wees tot 'n eersdaagse oorsig van die heersende toestande in ons gewone hospitale. Ons is daarvan oortuig dat ons opleidingshospitale gunstig vergelyk kan word met enige ander in die wêreld wat voortreflike voor- en na-operatiewe behandeling van pasiënte betref—verskeie verslae van lang reekse operasies skraag hierdie mening—maar die resultate aan gewone hospitale kan gerus binnekort in oorsig geneem word om 'n betroubare berekening van resultate te verkry; dit sal terloops onnodige pessimisme aan die een kant en oorbodige tevredenheid aan die ander kant, voorkom.

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RECENT ADVANCES IN AVIATION MEDICINE*

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Aviation medicine is that branch of medicine which is concerned with and related to the biology of flying. Research scientists of many disciplines, both in aeromedicine and related fields, are constantly striving to keep abreast of the demands made on human physiology by the performance factors inherent in modern high-performance aircraft.

Professionally, aviation medicine is classified under industrial medicine, in the sense that it is a highly developed branch of preventive medicine which, because of its military significance, is in a position to apply vastly expensive research programmes to the solution of its problems. In the United States it has in fact been elevated to the status of a distinct speciality, a lead which is certain to be followed by other countries. This recognition serves as an indication of the importance attached to its endeavours to keep human beings alive in the hostile environment of extreme altitudes into which modern high-performance jet and rocket aircraft are taking him. Man, who was designed for a terrestrial existence and is at best only a flying compromise, is confined by relatively narrow physiological limits of pressure, temperature and atmospheric composition. Modern aviation, however, requires him to remain fully functional at altitudes and speeds of a magnitude unheard of even a few years ago. Seeing him safely past these physiological and physical barriers is the abiding task of aviation medicine.

Historically, aviation medicine is the product of World War I, when a survey of the Royal Flying Corps in 1915 showed a non-effectiveness rate of 65% among flying personnel. Subsequent investigation revealed the familiar problems of altered barometric pressure, hypoxia, operational fatigue and temperature changes which even today are not completely solved, but it is significant that once these challenging problems were recognized and the appropriate action taken, the non-effectiveness rate dropped steeply to the insignificant levels of today despite the fact that the stresses and strains involved have multiplied many times. The most important factors responsible for this achievement and for the recent advances in aviation medicine are the concerted efforts of research workers in aeromedicine and the practical application of these techniques by the airforce medical officer, who by virtue of his training and experience has an appreciation of the limiting factors in the adjustment of the human body to flight. This knowledge is utilized at squadron level in an air-crew effectiveness programme, whose objective is their continued maintenance in the highest possible state of effectiveness under all conditions of flight. The scope of such a programme is very wide and involves the full application of the resources of aviation medicine to the operational requirements of all air crew.

The most critical problems in aviation medicine are naturally concerned with the protection of air crews against the hazards of exposure to flight at high altitudes and high speeds. Decreased barometric pressure involves the hazards of hypoxia, dysbarism, neurocirculatory collapse, hyperventilation, extremes of temperature, ozone toxicity and cosmic radiation. Very high speeds although not significant *per se*, produce stress mainly through the application of acceleration forces—linear, angular and radial—and by the production of excessively high temperatures creating the so-called 'heat barrier'. In addition it poses certain problems of reaction time, and also profoundly complicates escape from disabled aircraft.

With the advent of really high-performance jet and rocket aircraft capable of flying transsonically and at extreme altitudes, many of the problems of flight, and particularly of human control over these manned missiles, have become critical. It has been found that, despite the amazing range and flexibility of the physiological compensatory mechanisms, there are certain definite limits which may not be exceeded. Such a limitation is that imposed by a reaction time which, although adequate in terrestial situations, is unable to provide fast enough responses from the pilot to cope safely and adequately with control problems encountered in the speed ranges above Mach 2.

Velocity and Acceleration

Take the problem of pilots in two hypersonic aircraft flying at say 1,800 miles per hour, or approximately 1 mile every 2 seconds. They will have a closing speed on a collision course of 3,600 miles per hour. At these speeds, even with the best possible visual acuity of say 6/3 to enable them to see each other at maximum visual range, the pilots would be unable to react fast enough to avert a collision. This happens because their reflexes are transmitted at a mere 200 miles per hour and this is quite inadequate to cope with the necessary avoiding action. This again is due to the fact that the lag time in visual preception is appreciable, and at supersonic speeds it becomes critical in relation to the distance travelled. Under such circumstances, the sequence of events would be an initial latent period of perception varying from 0·03 to 0·3 seconds, during which time the aircraft has travelled nearly 1,000 feet. Then it takes 0·4 seconds from the time the other aircraft appears in the visual field until it is perceived by the pilot's central vision, and his own aircraft has gone another 1,200 feet. At this stage the pilot has only seen the approaching aircraft—it has not been recognized. Recognition time may vary between 0·65 and 1·50 seconds and another 3,000 feet will be covered. This means that from perception to recognition the aircraft has traversed more than 5,000 feet. Now add to this the time required to make a decision and to do something about it, which may take several seconds, plus the motor reaction time to transmit an impulse to move the control column, which in turn activates the control surfaces, which after another latent period will begin to overcome the flight of the aircraft in a straight line and turn it away to avert a collision.

By the same token pilots of two aircraft flying at supersonic speeds in opposite directions and emerging suddenly from cloud, may in fact see each other only after they have passed. Known as the 'coming-past interval', this phenomenon occurs where the sum of the closing speeds exceeds the speed of transmission of the visual images of the eye to the brain. It can therefore, be defined as the present perception of an

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event that has already occurred in the past. The problems resulting from these basic reaction-time limitations of human control can, however, be overcome by the installation of electronic devices which can react much faster than man in order to control the aircraft.

Accelaration. Probably the most important manifestation of speed which affects both the pilot and the aircraft is the component of acceleration. Experimentally it has been determined that the average healthy young pilot can tolerate up to 5 positive *g* for 5 seconds, 3 negative *g* for 3 seconds and 12 transverse *g* for 3 seconds before lapsing into unconsciousness. Various methods have been devised to improve the *g* tolerance of the pilot, which is a serious limiting factor in aircraft performance. Providing the pilot with ways and means of withstanding higher *g* loads will enable the aircraft to accelerate faster and turn more steeply and make it a more manoeuverable weapon system. The latest pneumatic anti-*g* suit is the best answer to the problem and provides automatically controlled counter-pressure over certain vital body regions like the abdomen and lower limbs, to prevent the pooling of venous blood under the influence of increased gravitational pull. This garment allows the pilot to exceed his natural tolerance by approximately 30% and makes the aircraft much more manoeuverable as well as decreasing pilot fatigue after multiple applications of *g* loads.

Heat Barrier. Another important aspect of high-speed flight is the production of excessively high temperatures as a result of heating due to friction and compression of air at the boundary layer. At the present stage of development this phenomenon presents the overriding bar to progress in the hypersonic speed region, both as regards the aircraft and the pilot. The rise in temperature can be expressed by the formula $t\text{C}^\circ = \frac{0{\cdot}85\ (v)^2}{100}$, where v equals velocity in knots. Therefore at 600 miles per hour the rise in temperature is 30 C° and it increases as the square of the speed. This is no theoretical problem, because there are in fact rocket engines in existence which are capable of exerting enough thrust to overcome the drag caused by area-ruled airframes and are therefore able to keep on accelerating indefinitely through the upper hypersonic speed ranges were it not for the metallurgical problems occasioned by this so-called heat barrier. Air conditioning, ventilated suits and elaborate refrigerating systems have therefore to be installed in the aircraft to prevent the ultimate incineration of the pilot, whose heat regulating mechanisms are otherwise unable to cope with the excessive cockpit temperatures at speeds in excess of Mach 3.

Escape from Aircraft

A secondary effect of high speed is to complicate the problem of escape from disabled aircraft. Even at the very moderate speed of 350 miles per hour it becomes physically impossible for the pilot to bale out safely, because he will almost certainly be flung against the tail assembly by the slipstream. An ejection seat actuated by an explosive charge was devised to enable the pilot to leave the aircraft in an emergency. Extensive research and many experiments showed that an acceleration of at least 60 feet per second was needed to propel the seat high and fast enough to clear the oncoming tail assembly by a safe margin. This required an accelerative force of nearly 20 positive *g*. which appeared to be far above the accepted black-out tolerance of 5 positive *g* which the average fit man can withstand for 5 seconds. However it fortunately proved that if the duration of application of this force is kept down to less than 0·2 seconds and the rate of onset of *g* is kept below 200 *g* per second per second the human body, properly strapped in on an ejection seat, could safely withstand this load. Refinements to this ejection technique and equipment, by the use of an 83-feet-per-second ejection gun, used in conjunction with a duplex drogue system, have now made it possible to eject safely from both ground level and at very high speeds.

Leaving the aircraft safely is, however, only half the problem, because at high speeds terriffic wind-blast effects are met with, causing very abrupt decelerations. At 500 miles per hour the impact pressure of wind blast at sea level is equal to 4·4 lb. per square inch, or about 3,200 lb. on the total body surface. Winds at Mach 1, or approximately 720 miles per hour, develop pressures of 9 lb. per square inch, or about 6,500 lb. over the total body surface. At 1,000 miles per hour this will increase to about 2,500 lb. per square foot or 12,500 lb. to the body area in the seated position. In spite of these fantastic primary impact pressures live supersonic ejections have been recorded in actual flight emergencies and the pilots have survived with relatively minor injuries. This problem forms the basis for the much publicized work of Colonel John Paul Stapp of the United States Air Force on the rocket sledge at Edwards Air Force Base. His object in exposing himself to the abrupt decelerations from 632 miles per hour to a dead stop in 1·4 seconds, thereby subjecting himself to more than 40 linear *g*, was to test the ability of the human body to withstand such decelerative forces under controlled experimental conditions. His work had the important practical result of proving that the pilot could reasonably expect to survive ejections at the subsonic and mildly supersonic speeds of current high-performance operational aircraft, and that the next step of providing capsular escape for the pilot could be deferred to the next generation of fighter aircraft.

This ultimate form of escape aid will probably be ejection within a pod or capsular type of enclosure as the logical means of overcoming the effects of wind blast, as well as other hazards of cold and hypoxia. The pilot might still be subjected to high deceleration for a relatively long time but in a stabilized vehicle the force and direction of deceleration would be predictable and could be withstood by the use of the conventional safety harness. The maintenance of pressurization by emergency pressure-oxygen equipment should increase the chances of survival over ejection into the airstream. Many other advantages are offered by this form of escape which are not found with ejection seats. Capsules may have parachutes, emergency kits and oxygen equipment as integral parts, thus removing from the pilot much of the cumbersome gear that is now required. Although such capsules are very complicated they are in fact feasible and prototypes are at present being tested by the USAF at Hurricane Mesa in the United States.

Having ejected safely and survived the primary blast effects and the rapid deceleration the pilot must still be freed either manually or automatically from his seat to deploy his parachute and float down to earth. Because he might be injured or rendered unconscious by spinning and tumbling in the airstream, barostatically controlled devices have been evolved to perform these vital actions for him. If ejection occurs at altitude his oxygen supply is switched to a bale-out bottle and he is allowed to 'free fall' to an altitude of 10,000

feet, where an aneroid device will actuate the parachute-release mechanism. There are many advantages in a free fall from altitude in preference to the open parachute descent. It includes less danger of entanglement with the aircraft, less exposure to low temperatures, and smaller oxygen requirement, but its main advantage is because parachute opening shock is much greater at higher than at lower altitudes. At 40,000 feet it is 4 times greater than at sea level, or equal to approximately 33 *g*. At 10,000 feet it is no more than 5 to 8 *g*. In practice serious injuries have resulted from a parachute-opening impact at altitudes exceeding 25,000 feet.

High Altitude

Hypoxia. In considering the aero-medical aspects of high-altitude flying the central problem concerns the lack of oxygen met with at altitude. Hypoxia is a syndrome that results from inadequate oxygenation of the tissues as the result of a decrease of the partial pressure of oxygen in the inspired ambient air. The symptoms are dependent on a series of variable factors like absolute altitude, rate of ascent, duration at altitude, ambient temperature, physical activity, and individual susceptibility and tolerance, but the inevitable end-result is a progressive descending depression of the central nervous system and a disruption of the psycho-motor functions, causing serious incapacity of the pilot and invariably leading to loss of control of the aircraft. To obviate this danger it has long been standard practice to provide an oxygen system to supplement the alveolar oxygen partial pressure. However, the phenomenal rates of climb inherent in the performance of turbo-jet aircraft can expose the pilot who is not fully protected against hypoxia to these symptoms in such an alarmingly short space of time that, despite the fact that hypoxia symptoms only occur above 10,000 feet, it has now become imperative for him to use oxygen from the ground up in all flights both by night and by day. The protection afforded by the oxygen system however, is not unlimited, for high-performance aircraft can comfortably exceed altitudes where the total ambient pressure is not as high as the partial pressure of oxygen necessary for the required normal 90 to 95% oxygen saturation of the blood.

A critical height occurs at 34,000 feet, where the barometric pressure is 187 mm. of mercury. At this altitude the pilot on 100% oxygen will have an alveolar oxygen partial pressure of 160 mm. of mercury, which is equivalent to the normal conditions at sea level. However, on exceeding 34,000 feet on 100% oxygen he will exhibit symptoms of hypoxia ranging through the undetectable to the compensatory, the disturbance, and ultimately the critical stage exactly as if the pilot were ascending above 10,000 feet without oxygen. The second critical height is reached at 45,500 feet, where despite the use of 100% oxygen the pilot will be as hypoxic as he would have been at 23,000 feet without oxygen. The equivalent critical heights with and without oxygen are shown in Table I.

TABLE I: EQUIVALENT CRITICAL HEIGHTS WITH AND WITHOUT OXYGEN

Stage	*Altitude in feet*		*Arterial oxygen-saturation %*
	Breathing air	*Breathing 100% oxygen*	
Indifferent	0′-10,000′	34,000′-39,000′	95-90
Compensatory	10,000′-15,000′	39,000′-42,500′	90-80
Disturbance	15,000′-20,000′	42,500′-44,800′	80-70
Critical	20,000′-23,000′	44,800′-45,500′	70-60

To overcome this difficulty, the latest pressure-demand oxygen regulator was introduced whereby oxygen is delivered to the lungs under positive pressure to a maximum equivalent to 8 inches of water. With this amount of positive pressure an increase in ceiling of roughly 5,000 to approximately 50,000 feet is possible, but its application is limited owing to the fact that it reverses the respiratory cycle with a passive inspiration and an active expiration against pressure, which is very difficult and fatiguing over long periods. In addition there is in any case a limited amount of positive pressure that the alveoli can safely withstand. Pressure breathing is therefore an expedient of limited value and it does not greatly increase the absolute ceiling, but it is a very useful and life-saving emergency procedure up to altitudes of 52,000 feet.

The reversal of the breathing pattern and respiratory cycle with pressure breathing tends to an increased respiratory turnover and hence to the development of the symptom complex of hyperventilation. These symptoms closely resemble those of hypoxia and it is virtually impossible for the pilot to differentiate between these two conditions, which may be described as cause and effect tending towards the same end-result—loss of control. It will be appreciated that the pilots of modern high-performance aircraft must have a fairly high level of physiological training and indoctrination to be able to avert disaster by taking the vital corrective action when they are overwhelmed by the symptoms of a respiratory emergency.

Decompression Sickness. At altitudes exceeding 30,000 feet the bizarre symptoms of dysbarism, or decompression sickness, are liable to effect an air crew, particularly if they stay above this altitude for several hours. The symptoms are due to the escape of gases normally held in solution in the body fluids. As the body is decompressed bubbles collect in the tissues and joint spaces, giving rise to severe and sometimes intolerable pain. Large joints become painful and may cause apparent paralysis, paraesthesias and pruritus develop, and uncontrollable spasms of coughing with visual and vestibular disturbances sometimes follow. Dysbarism, however, does not disturb consciousness or the higher mental functions, except if it is allowed to become very severe, when a profound neuro-circulatory collapse may follow, This is one of the most dangerous complications of flight at altitude, for spontaneous recovery is not possible and even with hospital care the outcome is usually fatal.

Pressurization. As modern aircraft have a service ceiling far in excess of 50,000 feet the only possible way for the pilot to achieve a high altitude is to make use of a counter-pressure suit or a pressurized cabin, i.e. by artificially surrounding the pilot with a pressurized environment which is equivalent to a lower altitude than the height at which the aircraft is actually flying. Cabin pressurization has the advantage that an adequate pressure differential will, within certain limits, maintain the cabin at a functional altitude where pressure breathing is not necessary. In South African Air Force Sabre 6 aircraft, for instance, a pressure differential of 2·75 lb. per square inch is employed, which is approximately equal to 160 mm. of mercury. In other words, at 38,000 feet indicated altitude the 'cabin' altitude is roughly 18,000 feet, where the

pilot is still quite comfortable on a normal oxygen-demand regulator system. In fact even when flying at 50,000 feet the cabin altitude will still be at a pressure which will not necessitate pressure breathing.

Ozone. Even cabin pressurization, however, is not the complete answer, because in the rarified air above 50,000 feet very large and heavy compressors are needed to maintain cabin pressurization. Between 60,000 and 70,000 feet the aircraft will encounter the ozone layer between the stratosphere and the ionosphere, and ozone in the cabin in concentrations of more than 6 parts per million under a pressure of 2·7 lb. per square inch has a fatal toxicity.

Explosive Decompression. Whilst cabin pressurization up to a certain altitude is a satisfactory solution, the attainment of higher altitudes requires an additional method of ensuring the survival of the pilot should cabin pressure be lost for any reason thereby causing explosive decompression. The result of such an explosion is to transport the pilot instantaneously from his artificial atmosphere inside the pressurized cabin to the actual altitude he happens to be flying at; for instance from, say, 32,000 feet to 55,000 feet in a split second. Now above 50,000 feet a given volume of gas will expand to 14 times its volume at mean sea level. Seeing that all the gases trapped inside the body in the lungs, gastro-intestinal and other cavities are subject to this expansion the pilot may be in danger of rupture of his alveoli, with subsequent air embolism, should the expanded gases not be able to escape freely.

To obviate this danger of sudden exposure to the hazards of extreme altitude the pneumatic counter-pressure suit was introduced. This garment is in effect a personalized pressure environment which is barostatically controlled and is instantaneously inflated to maintain adequate pressurization around the pilot's body, when explosive decompression takes place. This application of counter-pressure to the body in conjunction with emergency pressure breathing will give the pilot a reasonable chance of survival provided he is able to descend quickly to lower altitudes.

Space Flight

At an altitude of 63,000 feet, however, the total barometric pressure has dropped to a mere 47 mm. of mercury, which is equal to the water vapour pressure of the saturated gases in the blood-stream at the normal body temperature of 37° C. Exposure to this altitude would lead to boiling of blood in the vessels and filling up of the lungs with steam. This altitude is known as the 'space equivalent' because survival times at any altitude above 63,000 feet would be identical. From here onwards only 12% of the total blanket of the atmosphere remains and for all practical purposes space flight commences.

For this purpose all the aids to high flying previously mentioned become inadequate and a self-contained pressurised capsule is called for. This capsule is the essential basis for the space ships of the near future and, like the rocket motors which must be used for propulsion at altitudes of 80,000 feet and above, it is atmospherically independent and will carry its own oxygen supply. For short flights a number of oxygen cylinders is carried sufficient for the duration of the flight, but for long flights out into space, ingenious use can be made of photochemical processes whereby used oxygen is repurified for repeated use by the crew inside the capsule. The Department of Space Medicine at the USAF School of Aviation Medicine at Randolph Air Force Base in Texas have in fact built a capsule incorporating some space-ship features and have test flown it satisfactorily in a large decompression chamber at altitudes in excess of 100,000 feet. Flights in space present a series of physical and physiopsychological barriers which have still to be overcome before it can become a reality. In the ionosphere, for instance, there is the danger of a higher level of cosmic radiation which over long periods may have deleterious radiation effects on the body. Small meteorites moving at fantastic velocities above an altitude of 460,000 feet may penetrate the skin of the space ship and cause loss of cabin pressure with dire results, but mathematically the chances of such a collision is deemed to be remote.

Pilots flying above altitudes of 60,000 feet have recently reported a disturbing subjective sensation of being completely free of all earthly associations and this has been termed 'the breakoff phenomenon'. This overwhelming sense of detachment from the earth may adversely affect air-crew performance, but prior knowledge of this and other hazards will enable man to adapt himself even to the strange environment of space flight.

Zero Gravity. Yet another phenomenon to be encountered on these flights outside the earth's gravitational field is that of the 'zero-gravity state'. Experimental studies at the USAF School of Aviation Medicine have indicated that adequate indoctrination of pilots can overcome this hazard to some extent. Indoctrination can be achieved by flying zerogravity parabolas in turbo-jet aircraft at low levels to induce zero-gravity for periods up to 60 seconds. It has been found that spatial disorientation which threatens in the zero-gravity state can be successfully overcome by visual reorientation, or by providing a small acceleration component in flight to simulate 1 *g*.

It is evident from this brief review of some of the problems and the recent advances in the field of aviation medicine, that the amazing powers of adaptation of man aided by the devices provided by the researches of aviation medicine will in the near future finally enable him to break his bonds with the earth and to penetrate beyond the threshold of space.

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Southern African Cardiac Society. The programme of a Meeting of the Cape Province section of this Society held at Groote Schuur Hospital, Cape Town, on the evening of 20 March 1958, Dr. Maurice Nellen in the chair, was as follows: (1) A presentation of a case of Taussig-Bing Malformation, by Drs. G. Sutin and V. Schrire; (2) (*a*) A case of Patent Ductus Arteriosus with Pulmonary Hypertension in a patient with gross Kyphoscoliosis, by Dr. Louis Vogelpoel, and (*b*) Studies on the Pulmonary Function in the same case, by Dr. B. Kaplan; (3) A study of the Racial Incidence and Seasonal Incidence of Coronary Thrombosis at Groote Schuur Hospital, by Dr. V. Schrire.

PSYCHIATRIC ASPECTS OF HYPERVENTILATION *

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The close association between respiratory activity and emotion has long been recognized. Shakespeare's reference to 'the lover sighing like a furnace' contrasts strikingly with Coleridge's picturesque description of 'calm thoughts' being as 'regular as infant's breath.' Widely divergent emotional states such as joy, alarm and grief may be accompanied by changes in the rate, rhythm and depth of respiration. The gasp of fear, the mournful sigh of melancholy, and the bellow of anger, are phrases in our language which bear witness to this well-known relationship.

Of particular interest to the clinician is the phenomenon of over-breathing, the physiological changes accompanying it, and the symptoms attributable to these changes. Voluntary hyperpnoea leads to a reduction in the CO_2 tension of the alveolar air and a rise in the O_2 tension. Plasma CO_2 content falls, the alkalinity of the blood increases and a compensatory excretion of a more alkaline urine with a lower ammonium content occurs. The urinary volume and phosphate content increase; acetonuria is present and the blood lactate rises. The pulse accelerates and may become irregular, and cutaneous vasoconstriction is observed. Leucocytosis and hyperglycaemia have been reported. The blood flow to the brain is decreased and local cerebral anoxia results. There is slowing of the electro-encephalogram and enhanced excitability of the motor cortex to electrical stimulation.[1]

Accompanying these physiological changes are a wide variety of physical symptoms referable to any system of the body. Neurological symptoms include lightheadedness, giddiness, faintness, blurring of vision, tinnitus and headache. Feelings of unreality, sleepiness, emotional lability with foolish laughing or crying and intense anxiety may be experienced. Movements become clumsy and consciousness may be lost. Peripheral paraesthesias of fingers, toes and tongue and lips occur and may spread to involve the whole body, and the classical manifestations of tetany with fascicular muscular twitching and carpopedal spasm may supervene. Circulatory symptoms include palpitations, precordial pain, and cold extremities. Profuse sweating, increased frequency of micturition, abdominal distension, flatulence and aerophagy have been described.

Not uncommonly in the practise of internal medicine and psychiatry, patients present with symptoms conforming wholly or in part to those outlined above. Sometimes these patients complain of respiratory difficulties such as sighing, the inability to get enough air in, or a smothering sensation over the chest, but more often they are unaware of the fact that they are over-breathing until leading questions direct their attention to their respirations. They complain instead of some or many of the numerous symptoms attributable to over-breathing. Characteristically symptoms occur episodically, but in some cases continuing as distinct from periodic symptoms dominate the clinical picture. This, the hyperventilation syndrome, commonly occurs in the absence of organic disease and is usually labelled functional or psychiatric. Typically, the patient's symptoms can be reproduced by instructing him to over-breathe.

The purpose of the present paper is to describe the psychiatric manifestations in a group of 25 patients in all of whom symptoms and signs attributable to hyperventilation formed a prominent part of the symptomatology. In many the presenting symptoms were those ascribed to hyperventilation, while in others psychiatric symptoms of various kinds were to the fore. In all, however, physical symptoms caused the patient considerable concern and could be reproduced by over-breathing. The present psychiatric findings will be compared with others in the literature and an attempt made to assess the status of the hyperventilation syndrome in psychiatry. The diagnosis in these 25 cases embraced a wide variety of psychiatric conditions, as follows:

Psychoneurosis		
Anxiety state	11	
Hysteria	2	
Mixed	2	
	—	15
Character Neurosis ..		3
Psychosis		
Depression	2	
Schizophrenia ..	4	
Paranoid state	1	
	—	7

Psychoneurosis

In the patients suffering from anxiety states, symptoms attributable to hyperventilation occured mainly episodically and formed an important part of the acute anxiety spell or panic state. During these attacks the anxiety was at times free floating, but more often specific phobias such as fear of dying, of collapsing, of the heart's stopping, of choking or suffocating, and of losing control and going berserk, coloured the patient's mental state. Not infrequently resentment and hostility accompanied the anxiety and attacks of panic were likely to occur in situations where aggressive impulses were aroused. In many patients depressive feelings were present.

Case 23. A 42-year-old married man, a skilled instrument maker, presented with spells of acute anxiety accompanied by a sensation of lightheadedness, pins-and-needles of fingers, intense palpitations and sweating, a choking sensation, and the conviction that his heart would stop and he would die. This patient had always been anxiety prone and behind a façade of spurious independence strong dependent needs were present. Whenever his security or that of his family was threatened, anxiety would supervene. He was markedly ambivalent towards his children and resented intensely the demands they made of him which he considered excessive. This attitude appeared to be related to his own feelings as a child, when he felt deprived both materially and emotionally. In situations when his hostility was aroused, he entertained sadistic fantasies towards his wife and children and simultaneously became intensely anxious and developed symptoms attributable to hyperventilation.

Case 1. A 35-year-old married woman, whose presenting conflict concerned her relationship with her husband, an unstable unreliable individual, presented with attacks of palpitation, dizziness and faintness, pins-and-needles of fingers and hands, precordial pain, and the fear that she was having a heart attack. These episodes occured particularly when she was alone waiting for her husband to return home late at night. She alternately hoped that he would return quickly, then angrily entertained ideas that he had been injured or killed on his way home. The occurrence

* A paper presented at the South African Medical Congress, Durban, September 1957.

of these death wishes in consciousness was associated with anxiety, and hyperpnoea and its physical accompaniments.

Apart from the role played by hyperventilation in the acute anxiety spell in some patients diagnosed as anxiety states, little overt anxiety was present in others at the time when physical symptoms were prominent. In these, symptoms could be regarded as examples of affect equivalents in which the specific physical symptoms of anxiety occurred without the patient being aware of their affective significance.

Case 8. A 33-year-old married man complained of precordial pain, palpitations, a smothering feeling over the chest, pins-and-needles of the fingers and a lightheaded sensation with fealings of unreality. He denied feeling anxious, although mild phobic symptoms had been present in the past, referring particularly to heights and to travelling in lifts. His symptoms commenced soon after his marriage and his assumption of the responsible role of husband and breadwinner. He was the baby of a large family indulged by his mother and resentful of having to give up this favoured position. His symptoms became accentuated during his wife's pregnancy and after the child was born. He could not bear to hear the infant screaming, and at times would walk out of the house to get away from the cause of his irritation. In situations like these, although denying anxiety he would complain of the concomitant physical symptoms.

In 2 patients hysterical mechanisms were prominent. In these, attention-seeking motives were clearly expressed through their symptoms, and in both a past history of varied somatic pains and repeated operations was obtained. They described their symptoms in an histrionic manner and yet displayed no overt anxiety, which clearly had been converted into physical symptoms.

In 2 patients whose diagnosis is, psychoneurosis mixed, both anxiety and hysterical mechanisms were present.

Character Neurosis

In 3 patients features in their histories indicated their marked tendency to react psychopathically under stress. Difficulty in making stable interpersonal relationships, impulsive aggressive behaviour, recurring maladjustment in work situations, and failure to profit from experience, were typical of these patients. When behavioural and character disturbances of this nature are the predominant findings in a patient a diagnosis of psychopathic personality is indicated.

Case 3. A 34-year-old married man who complained of symptoms compatible with the hyperventilation syndrome, revealed in his history that his main difficulties were related to a severe character disorder. He had frequently changed jobs as he was unduly sensitive to criticism and at times distinctly paranoid. On occasion he would become actively hostile and aggressive; he would make impulsive decisions adversely affecting his family's security with little thought of the consequences. Time and again he would become involved in debt and soon after being helped out by a more affluent member of his family would repeat the same apparently purposeless behaviour and create new problems for himself.

Psychosis

In the psychotic group of patients, both depressive and schizophrenic illnesses were encountered. Again anxiety was the usual affective state, accompanying symptoms of hyperventilation, but in these patients the anxiety was of a psychotic nature.

Case 20. A 56-year-old married woman, always a timid reserved personality, had for some 3 months complained of increasingly severe and frequent attacks of palpitations, a heavy feeling in the chest, dizziness and lightheadedness, pins-and-needles and numbness of fingers and tongue, and bouts of loud belching. Apart from these periodic symptoms she became increasingly tired, listless and anorexic, and symptoms indicative of an endogenous depressive illness supervened. She would awake early in the morning and failing to get back to sleep would become more and more agitated. Depressive feelings were at their worst early in the day, lifting somewhat as the day wore on. Formerly interested in a variety of activities, she lost her zest for living and became convinced that she would never get well and that her end was near. Her preoccupation with her physical symptoms assumed near-delusional proportions and it was only after she had been treated by electroconvulsive therapy that the depression and the physical symptoms were relieved.

Among the 4 patients with schizophrenic illnesses, symptoms of hyperventilation were misinterpreted in a delusional way and bizarre explanations of their symptoms were offered.

Case 6. A 22-year-old commercial artist had for years been convinced that he had heart disease. Repeated reassurances from various doctors had failed to persuade him that he was wrong. From time to time he would experience feelings of unreality, giddiness, the fear that he was going to die, palpitations, sweating, and paraesthesias of his fingers and arms. These attacks he said were proof of his inferiority both physically and mentally. He was reticent and suspicious and expressed himself in a stiff disjointed manner. Ideas of reference were elicited and he complained of auditory hallucinations, the content of which included remarks about his gross mental and physical deficiency and derogatory whispers that he was homosexual.

Case 11. A 45-year-old widow had all her life been considered queer, sensitive, suspicious and quick to take offence. Since the death of her husband 5 years previously she had become prone to feelings of depression and preoccupied with physical symptoms. She felt unreal, as though in a dream, and at times a film would come down in her head. A constricting feeling around her chest prevented her from breathing properly and her hands and feet felt prickly and numb. She ascribed these symptoms to the fact that she was being hypnotized by her Native servants and was in constant fear that her home was about to be broken into and she and her children attacked. She misinterpreted actions and words of those about her and was paranoid in the extreme.

DISCUSSION

It is clear from the findings described above that a wide variety of psychiatric disorders is encountered among patients suffering from the hyperventilation syndrome. Reference to the literature suggests that the cases are loosely bound together as psychoneurotic or functionally disordered. Thus Kerr *et al.*[2] state 'this symptom complex while not seen exclusively among persons suffering from psychoneurosis is frequently found in them and its manifestations designated as anxiety states. Typically all the patients give a story of an encounter with some difficulty which causes emotional stress and anxiety.' Carryer *et al.*[3] observe that the syndrome occurs in tense, excessively anxious depressed or psychoneurotic patients. Gliebe,[4] while emphasizing the frequency with which hyperventilation may simulate organic disease, observes that hyperventilation occurs as part of a fear reaction in emotionally unstable people. Confronted by a situation in which he is inadequate the patient may transfer his anxiety to any organ by a sequence of physiologic changes consequent on hyperventilation. The importance of hyperventilation as a trigger mechanism in the precipitation of manifestations of hysteria is emphasized and the probability that hyperventilation contributes to the acute anxiety attack is mentioned. Edwards[5] describing a group of 63 patients says that all except 2 were considered to be individuals unusually sensitive to the tensions and conflicts of life and reacted to these conflicts with unjustified apprehension. In the majority of these patients the anxiety was free floating and chronic with more recent transference to fear of heart disease. Of the 2 exceptions, one suffered from a chronic personality disorder and the other had infective hepatitis. None of the patients were

psychotic. Lewis[6] points out that psychic features of varying nature and degree are the rule but may be masked. Anxiety, tension and apprehension are usually evident but in some hysterical subjects they may be concealed behind an inappropriate façade of apparent calmness. Engel[7] maintains that the hyperventilation syndrome may occur as a more or less non-specific reaction to the experience of terror, extreme anger, severe pain or other intense emotions, or it may be a symptom of neurosis. In anxiety attacks it represents the physical concomitants of the anxiety. A sensation of smothering or suffocation is common during anxiety and may produce over-breathing of which the patient is unaware. In other instances hyperventilation represents an hysterical conversion symptom effecting the relief of tension in a more symbolic way. In such instances it may represent the expression of a repressed wish for sexual intercourse or repressed hostility. Both mechanisms may be seen in the same patient. Dibden[8] considers the hyperventilation syndrome to be an expression of personality inadequacy. 'It occurs most often in patients with anxiety hysteria, in obsessive aggressive personalities.' Rome[9] states that patients with dyspnoea of psychological origin are often anxiety hysterics but that a large group consist of those patients whose symptomatic response to stress preferentially assumes this mode of expression.

The present findings and those culled from the literature suggest that commonly hyperventilation is associated with anxiety of varying intensity and kind. The affective state of anxiety and its physiological concomitants is met with in diverse psychiatric conditions. In anxiety states it is of course an outstanding symptom; but anxiety may be an important manifestation of schizophrenic and depressive illnesses too. In all these conditions symptoms attributable to hyperventilation may occur. In some anxiety states these symptoms contribute to the panic spell while in others they are affect equivalents in which the physiological concomitants of anxiety occur without the patient's being aware of their affective significance. In hysterical patients the symptoms express the patient's conflict in a more symbolic way and overt anxiety is not apparent. In depression and schizophrenia the anxiety is of a psychotic kind and symptoms of hyperventilation may be misinterpreted in a delusional way.

These considerations have important implications in the treatment of patients with this symptom complex. Some workers suggest that once the patient has been made aware of the nature and mechanism of symptom formation, and then reassured, lasting benefit will accrue. This approach no doubt is justifiable in individuals whose symptoms are of acute onset and related to a severe stress situation, and who have displayed few tendencies to react psychoneurotically in the past. It is well recognized that an anxiety state may vary from an acute self-limiting disorder to a chronic disabling condition requiring prolonged treatment. In the latter case symptoms will certainly not respond to simple reassurance and explanation. Similarly in patients with character disorders only intensive psychotherapy is likely to help, and even then benefit is uncertain. Similar considerations apply to patients with depressive or schizophrenic illnesses whose disorder must of course be treated appropriately.

Hyperventilation then is one aspect of the individual's anxiety reaction, and the mechanism whereby certain physical symptoms are produced in patients suffering from various psychiatric disorders. The diagnosis hyperventilation syndrome is an incomplete one, for a proper psychiatric diagnosis is always available and it is on this diagnosis that the efficient handling of these patients depends.

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CHOLECYSTECTOMY IN PATIENTS WITH CORONARY HEART DISEASE*

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That chronic cholecystic disease and coronary heart disease frequently occur in the same person is an accepted fact, and the possibility of an aetiologic relationship between the two has been the subject of wide speculation.[1] Many consider that the mere existence of gall-bladder disease has a deleterious effect on the heart. This opinion was strongly fostered by the writings of Babcock[2] at the turn of the century, and to this day many others share the view that gall-bladder disease causes 'irreparable cardiac damage'.

A survey of Babcock's cases, however, reveals the inadequate grounds on which such claims were based. Equally unsubstantiated are the claims that certain patients with angina pectoris have been completely relieved of their symptoms[3, 4] and that in others the coronary circulation has been improved by cholecystectomy for gall-stones as evidenced by the disappearance of abnormalities in the electrocardiogram.[5] In the former instance biliary pain was mistakenly considered to be angina;[6] in the latter instance the changing electrocardiogram is actually a reflection of the natural life-history of disease of the coronary artery. Every clinician has repeatedly followed the evolution of an abnormal electrocardiogram resulting, for example, from a myocardial infarction through intermediate stages toward and often to normal whether cholecystic disease was present or not. But these considerations do not alter the basic problem when a patient who has both diseases presents himself. A patient with gall-stones, whether they happen to be symptomatic or not at the time, may nevertheless experience biliary colic or acute cholecystitis, which can neither be predicted nor prevented by anything short of the surgical removal of the diseased gall-bladder. These explosive complications of cholecystic disease might well cause serious embarrassment

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to a patient whose coronary circulation is already compromised. Diminution in coronary blood and disturbances of cardiac rhythm have been demonstrated both in man and in animals when the biliary tract or other upper abdominal viscera have been acutely distended with a balloon.[7-10] The prevention, whenever, feasible, of the episodic complications of gall-bladder disease then assumes considerable importance for the patient with coronary heart disease.

Although the question of a possible aetiologic relationship between coronary heart disease and cholecystic disease must remain unanswered for the present, practical lessons can be learned from the analysis of the records of patients with coronary heart disease who have undergone cholecystectomy. Such a study was undertaken in 1955,[11] with essentially two questions in mind: How well do patients with coronary heart disease tolerate removal of a diseased gall-bladder? Does the removal of such a diseased gall-bladder influence the subsequent clinical course of the patient with coronary heart disease?

MATERIAL FOR STUDY

The records of all patients who had undergone cholecystectomy at the Mayo Clinic in the 5 years from 1948 through 1952 were reviewed. Those who had been given a diagnosis of coronary heart disease before operation were selected for special study. There were 100 such patients. The period selected was recent enough to judge the surgical risk in terms of antibiotics, anticoagulants and special procedures in anaesthesiology, and sufficiently remote to gauge survival rates. Cholecystectomy was performed on 5,891 patients during this period with an over-all mortality rate of 0·9% (53 cases). These figures represent all gall-bladder procedures, whether done for primary cholecystic disease or in the course of other intra-abdominal procedures. The age distribution is indicated in Table I. There were 64 males and 36 females in this series, a ratio which is more in keeping with the incidence of coronary heart disease than of gall-bladder disease.

TABLE I. AGE OF PATIENTS

Age (years)	*Total*	*Males*	*Females*
40—49	10*	5*	5
50—59	39	26	13
60—69	37	22	15
70—79	14	11	3
Total	100	64	36

* Includes one man 38 years of age.

CRITERIA FOR THE DIAGNOSIS OF CORONARY HEART DISEASE

The diagnosis of coronary heart disease was made on the basis of (1) a history of thoracic distress which conformed to the characteristics of angina pectoris (80%) and (2) a history consistent with previous myocardial infarction (31%) usually supported by a subsequent history of coronary insufficiency (angina pectoris or dyspnea) or electrocardiographically by relics of such an event, or by both.

The degree of coronary insufficiency was graded in accordance with the amount of effort the patient was able to tolerate. Only one patient gave a history of angina at rest; 46 patients experienced angina on mild to moderate exercise; 36 with more strenuous exercise; and 17 were asymptomatic on the programme which they followed. All 17 patients in the last category gave a history of previous myocardial infarction and 15 of them had significant electrocardiographic relics. No patients in the series had recently suffered from acute myocardial infarction.

The electrocardiograms of 29 patients were essentially normal; this figure corresponds closely to that reported in another series of patients with angina pectoris. For one patient no electrocardiogram was available. The electrocardiographic abnormalities of the remaining 70 patients are relics of anterior and posterior infarction, left ventricular hypertrophy, left bundle-branch block, right bundle-branch block, atrioventricular block and auricular fibrillation. Undoubtedly some of these changes were on the basis of hypertension.

CRITERIA FOR THE DIAGNOSIS OF GALL-BLADDER DISEASE

The diagnosis of gall-bladder disease was made on the basis of (1) a typical history of biliary colics (66%), with a history of jaundice in 19; (2) the occurrence of acute cholecystitis (6%), and (3) abdominal complaints ranging from mild dyspepsia to severe abdominal pain of atypical location or character in association with abnormal cholecystographic findings. In this series a non-functioning gall-bladder or a poorly functioning gall-bladder was as significant as the actual visualization of stones when the history was in keeping with a diagnosis of chronic cholecystic disease. Only one patient in the entire series was found to have no stones at operation.

The accuracy of the clinical appraisal of the gall-bladder status is reflected in the pathologic findings at the time of operation. As implied elsewhere, stones were present in 99 of these patients; common-duct stones were encountered in 20, and stones were found in the cystic duct in 10 other patients. The commonest finding in association with gall-stones was chronic cholecystitis, but in 6 cases the gall-bladder was acutely inflamed and was the cause of emergency admission to the hospital. In 10 other patients the gall-bladder was described as subacutely inflamed. Hydrops of the gall-bladder occurred twice in the series.

OPERATIVE AND POST-OPERATIVE COURSE

The usual routine operative precautions consisted of alerting the anaesthesiologist and the surgeon to the diagnosis of coronary disease. This simple expedient assisted in the choice of anaesthetic, usually a mixture containing a high percentage of oxygen, suggested that fluid should be administered cautiously, and warned the operating-room team to be more than ordinarily prepared to meet cardiac emergencies. Early ambulation was encouraged, and in some cases anticoagulants were employed.

Morbidity. The majority of patients experienced no difficulty at the time of operation; a mild to moderate drop in blood pressure was noted in 33 patients but this did not affect the operative or post-operative course. One patient in frank shock recovered uneventfully.

Auricular fibrillation developed at the time of operation in one case and 'an irregular pulse' in another. Frequent extrasystoles occurred in 2 patients. All subsided spontaneously.

The greatest single post-operative complication was thrombophlebitis; it occurred in 7% of patients. Wound infections, unexplained fevers and pneumonia each accounted for morbidity in 4%. There was one non-fatal myocardial infarction in the post-operative period. Two other patients experienced thoracic pain and showed electrocardiographic

evidence of temporary myocardial ischaemia; both recovered. In two patients non-fatal pulmonary embolism occurred and 3 had cerebral vascular accidents. Of the last, one died in hospital (case 3), one died a month after operation, and the third recovered.

Mortality: 3 patients died in the hospital after operation; all were males. A review of these three cases is enlightening.

Reports of the Fatal Cases

Case 1. The patient, a man 63 years of age, was obese and had mild hypertension. He gave a history, which was supported by electrocardiographic evidence, of myocardial infarction 5 months before admission. He had had no further angina, and the current electrocardiogram was normal. The patient had been subject to biliary colics without jaundice. The cholecystogram revealed a poorly functioning gall-bladder with stones. At operation a submucous leiomyoma of the stomach was found; it was removed along with the chronically inflamed gall-bladder containing stones. The operative course was uneventful but post-operatively the patient became oliguric and complained of pain in the right side of the chest. A gradual fall in blood pressure was accompanied by a rise in urea. The patient died on the 4th post-operative day. On post-mortem examination haemorrhagic pancreatitis was found and there was questionable early myocardial infarction.

Case 2. The patient, a man 72 years old, was admitted to the Clinic with the diagnosis of acute cholecystitis accompanied by jaundice. The patient had had angina with moderate exertion, and although he gave no history of previous infarction, the electrocardiogram showed right bundle-branch block and probably relic in the posterior part of the myocardium. During operation an irregular pulse developed and then subsided spontaneously. A stone was found and removed from the common duct. The pathologist reported subacute cholecystitis on chronic cholecystitis. The patient did well post-operatively until the 7th day, when a pulmonary embolus developed. On the next day he vomited blood. Thereafter his course was satisfactory until the 21st hospital day, when he complained of pain in the right side of the chest. He then had a convulsion and died suddenly. At post-mortem examination the patient was found to have pancreatic necrosis and an old posterior myocardial scar.

Case 3. A man, 79 years old, was admitted to the Clinic because of acute cholecystitis accompanied by jaundice. He had experienced angina on moderate exertion and gave a history of acute myocardial infarction 8 years previously. The electrocardiogram showed the relic of previous infarction. During operation the blood pressure decreased minimally. Acute ulcerative cholecystitis and a common-duct stone were found. Two days after operation, mild left-heart failure developed which responded to digitalis and the routine measures. On the 3rd post-operative day the patient had a cerebrovascular accident but seemed to be progressing satisfactorily until a low-grade fever developed which failed to respond to antibiotics. He died on the 17th post-operative day. Permission for post-mortem examination was not granted.

Of the 3 patients 2 were acutely ill on admission as the direct result of the complications of gall-bladder disease; 2 of the 3 patients died as a direct result of pancreatitis, which again must be regarded as a complication of the biliary disease. In one patient coronary insufficiency was a possible contributory cause of death. This is clearly a demonstration of the hazards inherent in chronic cholecystic disease regardless of whether it has been silent or whether it has been symptomatic.

FOLLOW-UP STUDIES

At the completion of this study, information regarding 95 patients was available. The survival curve for these patients as compared to the survival curve for the normal population of similar age and sex constitution was computed by actuarial methods. The 6-year survival rate was 70·7% as compared with 83·9% in the normal population. A direct comparison of the survival rate in this group of patients with the survival rate of the run-of-the-mill patients with coronary heart disease is of interest. In an earlier study[12] it was found that the 5-year survival rate among 6,882 patients with angina pectoris was 58·4%, a figure considerably lower than for the present series of patients; however, it is obvious that a direct comparison of these two groups cannot be valid inasmuch as the present series of patients constitutes a selected group of patients with coronary heart disease from which those with advanced degrees of coronary heart disease, those with congestive heart failure, and those with the more severe degrees of hypertension, were excluded. Certainly if some of these patients did live out their normal life expectancy, it might well be because they were spared the serious complications of chronic cholecystic disease.

As far as could be ascertained from the follow-up studies 6 patients died of subsequent myocardial infarction, 2 of cerebrovascular accidents, and 1 of hepatic coma; in 5 the cause of death was not known.

Information was available concerning the clinical course of 64 patients who were alive at the last inquiry. Of these, 36 reported no change in their cardiac symptoms; 17 were definitely improved and 11 were worse. The patient who had had angina decubitus pre-operatively was among the 17 patients who were definitely improved. From these data it is hardly justifiable to claim that cholecystectomy cures coronary heart disease.

SUMMARY

A study was undertaken to determine (1) the operative risk of cholecystectomy for patients with coronary heart disease and (2) whether removal of a diseased gall-bladder influenced the subsequent course of the patient with coronary heart disease. There were 100 patients in the series. The actual surgical procedure was well tolerated and there were no deaths or other serious complications on the operating table. Of these, 3 patients died in the hospital; one from acute pancreatitis on the 4th post-operative day, another from pancreatic necrosis on the 21st post-operative day after surviving a pulmonary embolus on the 7th post-operative day, and the third on the 17th post-operative day. The last-mentioned had cardiac failure and suffered from a cerebrovascular accident earlier in the post-operative course, neither of which seemed directly responsible for his death. Necropsy was not permitted in this case. The post-operative morbidity rate was not unusual for intra-abdominal procedures in patients of the age of these patients. One patient had an acute myocardial infarction after operation from which he recovered and 2 other patients showed clinical and electrocardiographic evidence of acute coronary insufficiency during their hospital stay.

The survival rate of this group of patients 6 years after operation was 70·6%, as compared with 83·9% in the normal population of similar sex and age constitution. This study establishes the relatively low risk of cholecystectomy in patients with symptomatic coronary heart disease and emphasizes the dangers inherent in the complications of chronic biliary disease itself. Such complications must be considered even more serious in patients with coronary heart disease. It is doubtful whether removal of a diseased gall-bladder influences the course of coronary artery disease directly but it is likely that life may be prolonged by preventing the serious complications of biliary disease by performance

of cholecystectomy, preferably during the quiescent phases of gall-bladder disease.

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RECENT TRENDS IN THE STUDY OF CORONARY-ARTERY DISEASE*

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The mounting incidence of coronary-artery disease in the past two decades in Britain, America, Canada and Western Europe and among South Africans has stimulated world-wide interest in the problem of causation with a view to providing measures to meet this challenge. Scientists in these and other parts of the world are engaged in intensive research and a vast literature has already been published dealing with many aspects of this problem. In the past an attitude of resignation to coronary disease prevailed because it was accepted as a natural development of the aging process. But, with the alarming increase of the disease in recent years and its occurrence in progressively younger age-groups, the problem of the aetiology has become urgent and has been receiving intensive consideration. The increase in the life-span of man must be taken into account when assessing the rapid upward trend of coronary disease since the beginning of this century. For example, figures quoted by White[1] indicate that the average age of 1,221 persons who died in Boston in 1829 was 25·2 years. In 1953 the average age of death in Boston was 69·5 years. Similarly Master's figures for the average life-span of the American from 1879 to 1899 was 34 years, whereas this increased progressively to 64·40 years by 1944 (Wood). It is obvious that one of the reasons for the lower incidence of coronary disease before the 1920s was the fact that many people did not live long enough to acquire coronary disease. There can, however, be little doubt that this increase in coronary disease is very real and cannot be attributed only to the longer span of man's life in the past few decades or the introduction of the wider use of the electrocardiograph and other methods employed in the more accurate diagnosis of coronary heart disease.

Dr. A. L. Agranat

Historical

It is of some interest to survey the history of coronary disease briefly and to present figures to prove that it has assumed a steep rise in incidence in recent years. The disease must have existed from time immemorial, the earliest evidence being indicated in the generalized atherosclerosis found in Egyptian mummies dating from 1580 B.C. There is very scant historical evidence to suggest that anything was known of the disease till the 17th century. In 1649, William Harvey described the vice-like paroxysms of chest pain which occurred in a knight who died in such a paroxysm—undoubtedly due to coronary thrombosis. Heberden's graphic description of angina pectoris in 1772, has remained a classic although he was not aware of the cause.[2]

The famous surgeon John Hunter was a victim of angina and, in his own words, 'his life was in the hands of any rascal who chose to worry him'. His fatal attack occurred in a fit of anger. His close friend, Jenner, of vaccination fame, performed an autopsy and concluded that his chest pains were due to calcification of the coronary arteries.

The 19th century brought very few advances in the recognition of this disease which must undoubtedly have taken its toll of life. This was probably due to the dogmatic statements made by leading clinicians of the day and accepted by their disciples without question. We find, for example, that Napoleon's personal physician, Corvisart, ascribed angina to a nervous disorder. His views were accepted in Europe, Britain and America for over 30 years. The famous pathologist Virchow believed that the scars he found in the heart in his post-mortem examinations were due to infection. A view was also prevalent that the coronary arteries were end-arteries, and that when an occlusion occurred in such a vessel, death was instantaneous and could, therefore, not have been preceded by any symptoms.

At the turn of this century, the great physician William Osler[3] remarked that the disease was 'not uncommon'—about 700 people dying annually of it in England and Wales. He commented that it was a disease of the better classes and not of the working classes and that a consultant in active practice would see about a dozen cases a year. He also mentioned that it was a rare disease in hospitals and that a case a year even in the large metropolitan hospitals in London was about the average. In Osler's series of 268 cases, including angina pectoris and coronary thrombosis, there were 33 physicians.

In 1912 James Herrick, of Chicago made medical history when he published a classic account of coronary thrombosis, but the First World War again delayed its general recognition till the 1920s. In subsequent years there was an increasing recognition of coronary disease, as shown by Cassidy's figures for Great Britain[4] (Fig. 1).

TABLE I

Year	*Number of Coronary Deaths*
1926	1,880
1936	14,095
1939	19,496

Other striking statistics are available to show the appalling increase in coronary disease. In 1926, 6·3% of all deaths in Great Britain from heart disease were attributed to this cause. In 1954 this figure had risen to 62·5%—an almost tenfold increase. American and British figures have shown an alarming increase in the mortality from coronary disease in the past 25 years and much more so during the past 10 years. Alarming, too, is the way in which it is creeping down to the younger age-groups—35 to 50 years—affecting chiefly men in the prime of life. South Africa is now considered to be level with the United States in having the highest incidence of coronary disease. Authorities have stated that as a single cause it accounts for the largest number of deaths after the age of 45 years and kills 4 out of every 10 European adults over this age. It has also been shown that the incidence of the disease among Europeans in Johannesburg is the highest in the Union. Table II shows the number of deaths due to coronary

* Valedictory Presidential Address, Johannesburg, 18 February 1957.

TABLE II. DEATHS FROM CORONARY THROMBOSIS (RATES PER 1,000)

Year	Europeans		Coloured		Asiatics		Natives		Mine Natives	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
1939–40..	155	·54	6	·24	4	·35	3	·02	1	·02
1940–41..	205	·74	4	·16	8	·70	9	·05	1	·02
1941–42..	197	·69	2	·08	8	·69	8	·04	1	·02
1942–43..	237	·81	1	·04	7	·59	10	·05	—	—
1943–44..	263	·95	3	·12	14	1·14	2	·009	1	·02
1944–45..	287	·93	9	·35	7	·55	15	·07	1	·02
1945–46..	289	·89	5	·21	12	·86	11	·04	4	·08
1946–47 .	309	·93	6	·25	15	·96	20	·06	1	·02
1947–48..	364	1·07	8	·35	8	·33	28	·08	1	·02
1948–49..	298	·87	12	·45	7	·42	25	·06	—	—
1949–50..	404	1·15	12	·44	13	·75	30	·07	1	·02
1950–51..	457	1·34	12	·40	24	1·22	25	·06	3	·07
1951–52..	439	1·27	11	·35	17	·82	40	·10	2	·05
1952–53..	461	1·32	12	·37	19	·88	28	·06	—	—
1953–54..	526	1·48	13	·39	23	1·05	52	·11	3	·08
1954–55..	534	1·50	16	·47	21	·89	60	·12	1	·02
1956	534	1·47	17	·46	26	1·04	30	·06	—	—

The last figures available of the total population of Johannesburg were 1,030,200: European 393,300, Native 561,600, Asiatic 28,700, Coloured 46,600.

The total death rate from infancy to old age in South Africa (White population) is approximately 8·5 per thousand. Of these 1·47 per thousand die of coronary-artery disease. This means that approximately 10 people die daily (babies to old age) in Johannesburg; of these approximately 2 people die from coronary heart disease daily.

thrombosis n Johannesburg from 1939 to 1956 and the comparison with Coloureds, Asiatics and Natives:

The Changing Pattern of Man's Life

Three points present themselves for consideration:

1. There is undoubted proof that coronary disease has taken a steep upward trend in the Western countries in the past 10-15 years.

2. Preceding generations were, to a great extent, less prone to coronary disease.

3. In Eastern countries, such as China and Japan, and among approximately 200 million Bantu in Africa, the incidence is extremely low.

A solution of the problem is being sought along comparative lines. The question arises: How did the mode of life of our ancestors differ from ours and did such differences have a bearing on the problem? Such differences, if pertinent, should also be applicable to differences in living customs between East and West. Factors such as racial characteristics and heredity, diet and physical activity, obesity and endocrine influences, smoking and the so-called 'stresses and strains' of modern life may play their part in this inquiry. The vastness of the problem calls for every effort to be made in an attempt to expose the factors responsible for the sudden increase in this disease.

In this intensive search for the cause, teams of biochemists, pathologists, physicians, statisticians and many other workers have contributed and are contributing a great deal in conjunction with important studies from an epidemiological approach. More and more publications are appearing and adding to the mass of literature already available from many parts of the world. It is worthy of note that research units have been established in this country in Cape Town and Johannesburg, where there is the unique opportunity of studying comparative race groups side by side.

At this stage I shall attempt to examine briefly the evidence on some of the changing features in the pattern and habits of the average European's life during the first half of this century.

Hereditary Factors and Racial Characteristics

The high incidence of coronary disease in America, Britain and Western Europe and among South Africans, and the comparatively low incidence in some Eastern countries and among the Bantu of the African continent suggest that racial characteristics operate in a great measure. This presents the question whether healthy or potentially unhealthy coronary arteries are inherited on a racial basis. It would suggest that the Japanese, Chinese or Bantu are, from the coronary point of view, in a much happier position than the European. On analysis certain objections can be raised against such generalizations. For example. in America there is, on the whole, no distinction in the mode of life among different national groups living in communities. Coronary thrombosis occurs with equal frequency among Americans of English descent and American Italians, Jews and Irish. The southern Italian and the Irishman have certainly not emigrated to America with a poor coronary-artery heritage. The defect has developed in America where a uniform way of living exists. In Chicago, for example, the American negro, who is a descendant of the African Bantu, has the same high incidence of coronary disease as the White American. The Americanized Japanese in Hawaii are subject to coronary disease to practically the same extent as the White Hawaians, although they are descendants of a race in which the disease has a very low incidence.

It is a well-known fact that the disease is almost equally prevalent among all the racial groups of European South Africans in contrast with the Bantu, in whom the disease is still a rarity. But it is significant that the urbanized Bantu, who is adopting European customs, is beginning to show increasing evidence of coronary disease. Another example of the weakness of the hereditary explanation is the significant decline during World War II in coronary disease among the Nordic and Anglo-Saxon peoples, in whom the post-war incidence has again risen steeply. These examples appear to indicate that hereditary and racial factors are not as significant or constant as they would appear to be and even when present can be reversed. Nevertheless, a genetic factor cannot be entirely denied, because of the common experience that coronary heart disease frequently occurs in families. But American statistics indicate that 30% of deaths over 40 years of age are due to coronary disease, which challenges the view that the disease is essentially a familial one.

Coronary Heart Disease in relation to Physical Activity

Interesting figures were published by Ryle and Russell,[5] who found that the mortality rate from coronary disease among professional groups was twice that of skilled artisans and 3 times that of unskilled workers. In this analysis of figures in England and Wales, physicians and surgeons head the list, with proprietors of wholesale businesses second, and the legal profession third. Morris *et al.*[6] carried out an extensive survey of coronary disease in relation to physical activity and inactivity. Their illuminating figures show that bus drivers have a higher incidence of coronary disease than bus conductors, and telephonists, whose occupation is sedentary, than the 'foot-slogging' postman.

During the past 3 or 4 decades there has been a striking diminution of physical activity among all classes of Europeans. This has been encouraged by the mechanization of industry and agriculture and the extensive use of the motor-car to replace the normal exercise previously derived from manual labour, walking and cycling. Even in the field of sport there is much more enthusiasm for watching games than for taking part, and it is doubtful whether the popular week-end sport indulged in by many professional men and office workers compensates for this change. This decline in physical activity during the past few decades has coincided with the sharp increase in coronary disease. It is possible that the motor-car is an important factor in the aetiology of coronary disease.

Endocrine Aspects

Up to 50 years of age the incidence of coronary disease in women is much less than in men, the ratio being about 10 to 1. The sex ratio from 50 to 60 years is approximately 3 males to 1 female. Only after the age of 70 years are the death rates from coronary disease equal in both sexes. It would appear that women whose pattern of living, in some important aspects such as their diet, is identical with that of men in the same community, must have some protective hormonal influence. With the spread of the disease into the younger age-groups this mechanism is becoming insufficient to protect some women in the thirties and forties from developing angina or coronary thrombosis. Experience in practice indicates that there has been a notable rise in the number of younger women with this disease. There is some evidence to indicate that oestrogen can reduce plasma cholesterol while androgens can raise this level. Fibrinolytic activity can also be retarded by oestrogen and accelerated by androgens. The possible value of oestrogen therapy must await the long-term control studies on patients with myocardial infarction.[7] An excess of thyroid hormone produces a diminution of the cholesterol level, whilst hypothyroidism increases it. Barr[8] has shown that cortisone may increase the cholesterol level, which would suggest that if used at all for myocardial infarction its use should be restricted to combating shock only. Oliver and Boyd[9] summarized their views on the hormonal influences of the circulating cholesterol by stating that the adrenal, thyroid and oestrogens produce a normocholesterolaemia and that the androgens and progesterone induce a hypercholesterolaemia.

Some evidence[10] has also been presented to suggest that 'stress' factors may stimulate the hypothalamus which, in turn, may increase the output of adrenaline, increase the prothrombin concentration, decrease heparin activity, and so accelerate clotting. In other words, it is suggested that a fit of temper may bring on an attack of coronary thrombosis in a susceptible individual. Endocrine factors appear to be important in the aetiology of coronary heart disease, but much work is still necessary to elucidate the exact relationship.

Smoking

Doll and Hill,[11] in their survey of cancer of the lung among doctors, have, incidentally, also produced figures to show that the incidence of coronary disease is about 1½ times as great in doctors who smoke as in non-smokers. Although there is no clear-cut evidence that smoking causes damage to the coronary vessels, a lurking suspicion of such damage remains in one's mind when one recalls the close association of smoking with thrombo-angiitis obliterans. Other reports[12] also support the view that smoking promotes coronary disease.

However, there is also evidence to the contrary. Coronary disease in the Bantu is rare, and in the Cape Coloured far less than in the Europeans,[10] yet there is no difference in the heavy smoking habits of the three groups. In the south of Italy the men smoke as much as those in the north, yet the incidence of coronary disease is much less in the south. In Japan, where coronary disease is very rare, heavy cigarette smoking is the custom.

Although it cannot be proved beyond doubt that there is a relationship between smoking and coronary disease, most patients who develop coronary thrombosis are usually heavy smokers, and this should be regarded as a warning.

Psychological Factors

Factors such as ambition and drive, the striving after economic and social success, frustration or contentment at work, domestic bliss or jarring, emotional reactions to environment, equilibrium or tension, still await assessment. Do these factors operate through the hypothalamus and so produce endocrinological effects? What appears fairly obvious is the frequent association of the 'stresses and strains' in the higher socio-economic levels among professional men and business executives, who, incidentally, have the highest incidence of coronary disease. It is difficult to dissociate stress factors from coronary thrombosis.

Obesity

In practice one is not impressed with a particularly high incidence of coronary thrombosis in the obese. On the contrary, most of the victims are of normal build and a fair number are thin. Ancel Keys[10] has calculated that over 95% of coronary deaths in America have not had their insurance premiums loaded on account of obesity. Under 50 years of age there is some evidence that there is a proportionate increase in coronary heart disease in obese people. In passing, it may be noted that obesity is not uncommon among the Bantu with little coronary disease. The fact that there is no considerable increase of coronary disease has no bearing on the accepted view that obesity is a hazard to good health. Some distinction may be made between endocrine obesity and that due to over-indulgence. The latter type carries a greater risk of coronary disease.

Diet and Fat Metabolism

This subject has received the greatest amount of attention and appears to be the most important one from the aetiological point of view. In general, the higher incidence and exceptional increase of this disease has occurred among Europeans all over the world who consume luxury diets, i.e. high in calories and fats. Ancel Keys conceived the idea of an epidemiological approach to the problem of coronary disease and must be regarded as the real pioneer of this work. In looking East it is apparent that the Chinese and Japanese are not prone to coronary disease, and the same applies to the Bantu of the African continent. One of the dominating contrasting features is the difference in diet. The American, the Englishman, people of Western Europe, the North Italian and the European in South Africa feed well; their diets are generous in calories and, in many countries, the fats comprise 40% or more of these calories. The Japanese and Chinese eat frugally and consume little fat. The African Bantu lives chiefly on maize and carbohydrates, with little protein and even less fat. Here, then, a striking difference in the diets of two large sections of the world's peoples has been observed, with a marked difference in the relative incidence of coronary disease. Ancel Keys[13] studied the fat metabolism in surveys covering numerous groups of people in different countries; he did this by estimations of the serum cholesterol and then enunciated two rules from his epidemiological studies. Firstly, whenever a population has a relatively high cholesterol level for middle-aged healthy men, a relatively high incidence of coronary disease is exhibited in such a group. These cholesterol studies were made in cities in America, England, Sweden and Italy, and also in Cape Town. Secondly, in his survey among the poor in southern Italy, the indigenous peoples of Nigeria, the Yemenite Jews, the Japanese, and the Bantu in Cape Town, he found a low incidence of coronary disease. That cholesterol levels in communities may be influenced by the variation of the percentage of fats consumed was convincingly demonstrated during World War II. In Great Britain, Holland, Denmark, Sweden, and particularly in Finland and Norway, the mortality from coronary artery disease was diminished in proportion to the percentage reduction of fats in the diet.[13]

Significance of Increased Cholesterol Levels

Over a hundred years ago cholesterol was found in atheromatous plaques, and its significance in coronary-artery disease has never been disputed. The problem which has faced the biochemist and the pathologist is how this lesion occurs in the coronary vessels. The solution to this question is still being eagerly anticipated because it may provide the answer to the disease. In the meanwhile we must apply the information which is available, although it is still inadequate.

It should be appreciated that the average level of the serum cholesterol in a community is regarded as an index to the incidence of coronary disease. Serum-cholesterol levels are not influenced by the amount of cholesterol ingested in food, but are dependent on the quantity of fats consumed. By an intricate biochemical mechanism, cholesterol becomes embodied in the various fractions of the metabolized fat—chiefly in the alpha- and beta-lipoprotein fractions of the circulating lipids. The raised serum-cholesterol level is significant because it usually reflects disturbances in the general lipoprotein pattern[14–18] and not because the cholesterol itself is raised. In other words, it is a convenient measure of potential or established coronary disease in community surveys, while at the same time it has limitations in individual interpretation.

Clinically, essential hypercholesterolaemia provides a good example of disturbed cholesterol metabolism. From the laboratory aspect there is usually an abnormally high serum cholesterol associated with an abnormal lipogram and, clinically, about 80% of these patients develop ischaemic heart disease, usually at an early age.[18] Gross disturbance of fat metabolism also occurs in the well-known condition idiopathic hyperlipaemia, in which the raised serum cholesterol is incidental and the important laboratory evidence is the high lipid content due to an increase in the neutral fats and lipids, which give the serum a milky appearance. This condition is also associated with an extremely high incidence of coronary disease.[19,20]

A raised serum cholesterol is not so significant when it is not associated with a disturbed lipogram in such diseases as, for example, nephrosis,[21] myxoedema,[22] and biliary obstruction.[23]

Population surveys have been carried out in communities in many parts of the world to determine the average serum-cholesterol level in relation to coronary disease. Keys has surveyed population groups in Italy, Sweden, America, Nigeria and the Far East, and the constant and significant finding is the higher the average serum-cholesterol level in a community, the higher the incidence of coronary disease. In South Africa, where the special advantage of studying race groups side by side exists, a number of important surveys have also been made. In Johannesburg, Bersohn and Wayburne[24] have studied the serum-cholesterol levels in newborn African and European infants and in mothers. They found that the cholesterol levels in the two groups of infants were identical, but that the European mother invariably showed a considerably higher level than the African mother. Although the European infant begins life without a 'cholesterol handicap', this advantage is not maintained, for the level rises steeply with age, as demonstrated by the work of Adlersberg *et al.*[25] and Walker and Arvidsson,[26] and in the Cape Peninsula by Bronte-Stewart *et al.*[27] Walker and Bersohn[28] have confirmed the fact

'that the lipoprotein pattern of the Bantu remains young'. In South Africa, as elsewhere, the population surveys indicate that raised serum cholesterol in the European is associated with a high occurrence of coronary heart disease.

The question of fat metabolism in relation to atherogenesis of coronary disease is extremely involved, and the highly technical laboratory studies are outside the scope of the average physician. These problems await further elucidation by the laboratory workers in this field. The work now proceeding in many centres, including those in South Africa, promises results in this important field of fat metabolism. In the meanwhile, on the basis of the evidence available, the clinician may reasonably accept the view that a raised serum cholesterol predicts the probability of coronary disease.

SUGGESTED MEASURES TO REDUCE THE INCIDENCE OF CORONARY DISEASE

At this stage, with the mass of undigested information, and views based on many divergent theories and immature conclusions, such a heading as 'prevention of coronary disease' may appear to be unjustifiably ambitious. Nevertheless, the clinician is faced daily with the growing problem of the scourge of coronary disease and, aware of his obligations to his patients, must attempt to decipher some pattern of advice from the information available on reasonable, if not on dogmatic, grounds. It is essential, however, to realize the limitations imposed by the present state of our knowledge.

Prevention of coronary disease is a recent concept and may at this stage be considered from 3 aspects, viz. (1) environment, (2) dietetic hygiene and (3) drugs. *Environmental Factors* will include advice in respect of regular and sufficient exercise, strict moderation in smoking, ample recreation and rest. Psychosomatic factors are more difficult to control because they are linked up with the striving for economic and social success and the highly competitive trends in modern life. Nevertheless, when the probable penalty for immoderate living is appreciated by the individual, a measure of cooperation may be anticipated.

Dietetic Factors

To quote Ancel Keys[10]: 'No major primary role in atherogenesis or in the prevention of clinical coronary disease can be assigned to race, nationality, obesity and overweight, cigarette smoking or indulgence in alcohol. Some of these factors may make a secondary contribution, perhaps contingent upon the existence of a particular set of circumstances'. He is, however, not prepared to minimize the influence of physical activity. He continues: 'When we come to the diet, apart from sheer calories, there is much firmer ground to conclude that it is of major primary importance. The evidence is consistent in theory, in field studies, in statistics and in experiments, both on man and animal'. Replacing the saturated fats, such as the animal and hydrogenated vegetable fats, with highly unsaturated fats derived from vegetables and some fish oils, or even adding these unsaturated fats to a normal fat intake, will reduce the total plasma lipids and serum cholesterol in most people.

Interpreting the importance of diet in its practical application, the course to be followed is a general reduction in calorie intake, with not more than 20-25% of calories to be provided by fats, and the utilization of *unsaturated* with a minimum of saturated fats. While the advice to 'cut down fats' may in general terms be sound for patients with established or threatening coronary disease, specific diets should be provided. Such diets are available

TABLE III

Fat	Saturated	Mono-ethenoid	Poly-ethenoid
Butterfat	57	39	4
Coconut oil (hydrol)	97	3	0
Corn oil	12	37	51
Cotton-seed oil	25	25	50
Lard	43	—	10
Margarine	65	25	10
Sardine Oil	23	23	54
Sunflower-seed oil	10	28	62
Tallow (beef)	53	—	4
Olive oil	12	—	12

and should clearly indicate the foods which are allowed or prohibited. In addition, a table should be provided showing the exact content of unsaturated and saturated fats in oils and fats commonly used in household cooking. with the strict injunction that those with a high percentage of saturated fatty acids shou!d be avoided as far as possible. Table III an example of such a table, adapted from the studies of Ancel Keys[10]:

Additional dietary changes should include the replacement of white bread by brown bread, coarse cereals such as wheat, oats and maize, which have a high content of coarse fibre and cellulose, vegetables, potatoes and legumes. McCance in Cambridge and Walker in Johannesburg (quoted by Walker and Bersohn)[28] have reported that large amounts of fats, up to 22 g. daily, are voided in the stools of those who consume large amounts of these coarse foods: This is in striking contrast with the very small quantity, approximately 1 g. of fat voided in the stools of those who consume a low-residue and high-fat diet.

Not only sufferers from coronary-artery disease, but also those who are prepared to make a conscious and serious effort to try and avoid becoming victims of this scourge should follow such a dietetic regime. It would not be overstating the case to warn people that rich, fatty foods may in due course 'silt up' the coronary arteries in much the same way as an over-rich petrol mixture will carbonize the cylinders of a motor-car. There is encouraging evidence to indicate that a strict and sustained low-fat, moderate-calorie and high-cellulose diet may retard the formation of atheromatous deposits in the coronary arteries. Atheromatous plaques produced experimentally in rabbits or chicks on a high cholesterol diet may be made to regress by removing the dietary cause. Although it may not be possible to infer that the same change would occur in man, it has been claimed that the cutaneous xanthomata due to cholesterol deposits on the skin may be made to regress somewhat on a low-fat diet.[30] This theory of clinical regression of coronary atherosclerosis receives further support from the relatively low incidence of severe atherosclerosis in autopsy findings in emaciated individuals who have died from cancer.[13] The prophylactic approach to coronary heart disease receives logical encouragement from these facts.

The modern trend in the dietetic approach is a valuable contribution in the field of prophylaxis in coronary-artery disease, although there are still many gaps in our knowledge. There are, of course, other views expressed by nutritional experts and others, as for example the opinion that atherogenesis may be caused by a threefold vitamin deficiency of essential fatty acids, vitamin E, and vitamin B6,[31] caused mainly by the artificial processing of foods. Future developments will, no doubt, clarify the association, if any, of vitamins, proteins, carbohydrates or minerals with the process of coronary-artery damage. We should also appreciate the important evidence available that atherogenesis is initiated in early life through the over-feeding of children by over-zealous parents. It is not surprising, then, that such a high incidence of coronary atheroma was found amongst the young US soldiers killed in the Korean War.

Drug Treatment

No drugs are known to have any beneficial effect on the atheromatous plaques in the coronary vessels. At present drug treatment is aimed at diminishing either the cholesterol level or the coagulating factors of the blood. Trials with triiodothyroacetate have failed.[32] High-dosage nicotinic-acid therapy produces variable results on the cholesterol level and is a cumbersome treatment, although concentrated preparations are now available. The oestrogens have been withheld on account of their obvious disadvantage but evidence of their probable value may yet be forthcoming. At present the beta-sitosterols which are said to reduce the cholesterol levels are being tried with some measure of success.[33]

From the prophylactic aspect, the anticoagulant drugs may be of considerable value. 'Physiologic clearing process' of lipids by heparin several hours after the ingestion of a fatty meal is well recognized.[34] The rapid excretion of heparin, the need for parenteral therapy, and the usual extensive bruising, limit heparin administration to short periods or long intervals. Long-term treatment with dicoumarol or similar drugs has been advocated for prophylaxis against recurrent attacks of coronary thrombosis.[35,36] My impressions of the long-term dicoumarol treatment of a large series of cases over a number of years are that this treatment is of considerable prophylactic value. Nevertheless, a further assessment of its value is necessary. During Prof. Melville Arnott's visit to South Africa last year he informed me that an extensive investigation, with a control series of cases, was being initiated in Great Britain under the auspices of the Medical Research Council. This should provide valuable information for the

prophylactic use of dicoumarol in preventing recurrence or threatening attacks of coronary thrombosis.

In conclusion, I would again remind you of the urgency and importance of the problem connected with the steep rise in coronary-artery disease as illustrated by the history of this condition and the alarming statistics in all Western countries, no less in South Africa and not least in Johannesburg.

Heredity, race and obesity do not appear to be consistant factors in this sharp increase. There is evidence that female sex hormones have some protective effect and that the androgens increase vulnerability, but Ancel Keys has assured us 'that being a male is not necessarily fatal'. Linked with the hormonal influences are the psychosomatic factors which play an obscure role in the aetiology depending on a tense or peaceful mode of living. Although alcohol has not as yet been mentioned, it has been stated that, for unexplained reasons, heavy drinkers tend to have a low serum cholesterol and a correspondingly low incidence of coronary disease.[37] With reference to physical activity, the evidence seems to indicate a considerably increased incidence of coronary disease in sedentary occupations. In view of the vast amount of research work now proceeding, the prospects of improving prophylactic measures in the future are very promising.

To avoid the threat of coronary disease as far as possible one should follow, not the precept of Horace, 'To-morrow do thy worst, I have lived to-day', but that of the old Latin proverb, 'Not as it pleases us but as it is right for us—so let us live'.

I should like to thank Dr. I. Bersohn, of the South African Institute for Medical Research, for his advice and assistance at all times. My thanks are also due to Dr. J. W. Scott-Millar, Medical Officer of Health for Johannesburg, for providing me with the table of deaths due to coronary thrombosis.

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IN MEMORIAM

CHARLES PETRUS THERON, B.A., M.B., CH.B.

Dr. J. N. W. Loubser, Bethlehem, O.V.S., skryf: Die skielike dood van dr. C. P. Theron aan 'n kransslagaartrombose op 31 Maart 1958 was 'n geweldige skok vir die plaaslike gemeenskap. Hy is op 5 April 1880 op Bethlehem gebore as die oudste seun van ds. en mev. Theron van die N.G. Kerk. Sy skoolopleiding het hy op Bethlehem en Wellington, Kaap, geniet en is daarna na Sacs, Kaapstad, waar hy in 1901 sy B.A.-graad, met lof, verwerf het. In 1902 is hy na Edinburgh, Skotland, om in die medisyne te studeer. Dat hy 'n knap mediese student moes gewees het, blyk uit die feit dat gedurende sy studentejare nie minder as drie bronsmedaljes aan hom toegeken is vir „Junior Anatomy' in 1903, vir „Systemic Surgery' in 1904 en vir „Junior Surgery' in 1906. Nadat hy sy M.B., Ch.B.-graad in 1907 verkry het, het hy nog in dieselfde jaar na Suid-Afrika teruggekeer en diens aanvaar op Kakamas, destyds 'n arm-blanke nedersetting van die N.G. Kerk, waar hy tot 1911 werksaam was en hom toe op Bethlehem, as Algemene Praktisyn, gevestig het. Daar ek reeds twee jaar tevore hier begin praktiseer het, het ek dus die voorreg gehad om hom as kollega en vriend vir byna 'n half-eeu intiem te ken.

Charles Petrus Theron

Charlie Theron was iemand met 'n buitengewoon hoë pligs- en diensbesef; diens aan sy siek medemens, diens aan die minderbevoorregtes (veral kinders) van die gemeenskap, diens aan die professie en diens aan sy geboortestad, Bethlehem. Daar was haas g'n opvoedkundige, kulturele, professionele of maatskaplike liggaam of vereniging waaran hy in die loop van jare nie 'n lid of die voorsitter was nie. Vir 35 jaar het hy as stadsraadslid gedien en was nie minder as tien keer burgemeester nie. Sy troetelkind egter was die Charlotte Theron-Kinderhuis vir wie hy alles feil had en vir wie geen finansiële offer vir hom te groot was nie. Dit was 'n inrigting wat sy moeder net na die Anglo-Boere-Oorlog, onder baie moeilike omstandighede, vir oorlogwesies gestig het en wat in die loop van jare tot 'n pragtige groot inrigting gegroei het vir die huisvesting van byna 400 verwaarloosde kinders. Vir byna 'n halfeeu lank het hy daagliks die klein inwoners van hierdie Kinderhuis besoek en medies versorg, sonder enige geldelike vergoeding en nog die dag voor sy dood was hy daar op huisbesoek. Dit is voorwaar 'n prestasie wat m.i. nie maklik oortref kan word nie en dit het my altyd verbaas hoe vanselfsprekend hy dit alles beskou het.

In die werksaamhede van die Mediese Vereniging het hy altyd baie belang gestel en was in 1928 een van die 14 stigterslede van die N.O. Afdeling van die O.V.S.-Tak, wat vandag 97 lede tel, van wie hy nie alleen die oudste, maar ook een van die getrouste ondersteuners was. In 1930 het sy voorsittersrede, oor die onderwerp „Why do my patients leave me'? hom nie alleen die Hamilton Goue Medalje, van die S.A. Tydskrif vir Geneeskunde vir die verdienslikste publikasie van die jaar besorg nie, maar dit is ook deur talle oorsese mediese tydskrifte, in 'n halfdosyn of meer tale, oorgeneem en in 1950 weereens, op spesiale versoek van lede van die Vereniging, in ons mediese tydskrif herdruk.

Hy het aan nie minder as drie oorloë deelgeneem nie. In die Anglo-Boere-Oorlog het hy as jong Vrystaatse burger met die geweer in die hand geveg; in die eerste Wêreld-Oorlog het hy aangesluit by die S.A.G.D. en weereens (op 62-jarige leeftyd!) tydens die tweede Wêreld-Oorlog en was toe van 1942 tot 1945 met die rang van kaptein in die militêre hospitaal op Voortrekkerhoogte werksaam.

Hy was drie keer getroud. In 1908 met mej. Joey le Roux van

Franchhoek, wie hom in 1931 ontval is. Uit hierdie huwelik is een seun gebore, wat tans as radiologiese spesialis op Johannesburg praktiseer. In 1934 is hy vir die tweede keer getroud met 'n mev. Miemie Steyn, wat egter reeds in 1936 oorlede is. In 1945 is hy met mej. Nonna Kok van Bloemfontein getroud en uit hierdie huwelik is daar 'n seun gebore wat nou tien jaar oud is.

Charlie Theron was by uitstek 'n vegter, ja, selfs 'n gedugte vegter as dit gegaan het om 'n ideaal of 'n saak wat hom na aan die hart gelê het, maar ek kan met alle opregtheid getuig dat in al die jare wat ek hom geken het, ek nooit 'n persoonlike vyand van hom teengekom het nie en kan dit alleen daaraan toeskrywe dat hy die rare gawe besit het om nooit die persoon met die saak te verwar nie.

Ten tye van sy dood was hy lid van die Uitvoerende Komitee van die S.A. Kankervereniging, asook waarnemende stadsgeneesheer. Sy stokperdjie was die beoefening van die skilderkuns. Ook het hy groot belang in musiek gestel en was vir baie jare voorsitter van die plaaslike musiekvereniging.

Die hoogagting en waardering van sy kollegas en van alle klasse en rasse van die gemeenskap wat hy steeds geniet het, was ruimskoots verdien weens sy minlike persoonlikheid, sy hulpvaardigheid en voorbeeldige etiese gedrag as dokter en mens. Sy dood laat 'n leemte in die professie en in die samelewing wat nog lank gevoel sal word.

Aan sy gade en twee seuns wil ek hier graag my innigste meegevoel betuig.

PASSING EVENTS : IN DIE VERBYGAAN

The National General Practitioners Group, Cape Western Subgroup. The annual general meeting of the sub-group will be held on Wednesday 30 April at 8.15 p.m. at Medical House, 35 Wale Street, Cape Town.

Uniale Groep van Algemene Geneeshere: Onderafdeling Wes-Kaapland. Die algemene jaarvergadering van die onderafdeling Wes-Kaapland sal in Mediese Huis, Waalstraat 35, Kaapstad, op Woensdag 30 April om 8.15 nm. gehou word.

* * *

Mr. Arthur J. Helfet, of Cape Town, has left to attend the Joint Meeting of the British Commonwealth and American Orthopaedic Associations which will be held in Washington in May. He will give one of the Trinity Term Orthopaedic Lectures at the University of Oxford on his way back in June.

* * *

Research Forum. The next meeting of Research Forum, University of Cape Town, will be held in the A-Floor Lecture Theatre, Groote Schuur Hospital, Cape Town, on Wednesday 7 May at 12 noon. Speakers: Dr. H. Gordon, Prof. J. F. Brock and Mr. J. Wilkins. Subject: 'Dietary factors and serum cholesterol with especial reference to non-fat substances.'

* * *

The Nuffield Foundation Dominion Travelling Fellowships. The Council for Scientific and Industrial Research publish a notice received from the Nuffield Foundation South African Advisory Committee concerning Dominion Travelling Fellowships for the year 1959. Two fellowships are offered in the Natural Sciences, one fellowship in Medicine, and one fellowship in the Humanities; an additional fellowship may be awarded in any one of these fields. Applicants should normally be between 25 and 35 years of age, have high intellectual and personal qualities, and have shown capacity of an unusual order for advancing knowledge and education in their fields. They must undertake to return to South Africa as soon as possible after the termination of their fellowships. Copies of the regulations and application forms may be obtained (*a*) *By university applicants*, from the Registrars of their universities, and (*b*) *By others*, from the Honorary Secretary, Nuffield Foundation, South African Advisory Committee, c/o University of the Witwatersrand, Johannesburg. Applications received after 30 April 1958 will not be considered until 1959.

* * *

Unie van Suid-Afrika. Departement van Gesondheid. Aangifte van gedugte epidemiese siektes en poliomiëlitis in die Unie gedurende die tydperk 28 Maart tot 3 April 1958.

Pes, Pokkies: Geen.

Tifuskoors. Kaapprovinsie: Een (1) Naturellegeval in die St. Marks-distrik. Drie (3) Naturellegevalle in die Steynsburg-distrik Bekragtig deur laboratoriumtoetse. Alle voorsorgmaatreëls getref.

Poliomiëlitis

	Bl.	*Nat.*	*Kl.*	*As.*	*Totaal*
Transvaal	3	5	–	–	8
Kaapprovinsie ..	–	3	–	–	3
Oranje-Vrystaat ..	–	–	–	–	–
Natal	1	–	–	–	1
Totaal ..	4	8	–	–	12

Local Authorities		*Eur.*	*Non-Eur.*
Transvaal:			
Alexandra Township	U		1
Balfour District	R	1	
Bronkhorstspruit	R	1	
Ermelo District	R		1
Germiston District	U		1
Lichtenburg District	R		1
Pretoria Municipality	U	1	
Vereeniging Municipality ..	U		1
Cape Province:			
Port Elizabeth Municipality ..	U		3
Natal:			
Amanzimtoti Borough	U	1	

U = Urban. R = Rural.

* * *

Union of South Africa. Department of Health. Notification of formidable epidemic diseases and poliomyelitis in the Union during the period 4-10 April 1958.

Plague, Smallpox: Nil.

Typhus Fever. Cape Province: Two (2) Native cases and one (1) European case in the Municipal Area of Steynsburg. Confirmed by laboratory tests. All precautions taken.

Poliomyelitis

	Eur.	*Nat.*	*Col.*	*As.*	*Total*
Transvaal	–	–	–	–	–
Cape Province ..	–	3	2	–	5
Orange Free State	–	–	–	–	–
Natal	1	–	–	–	1
Totals ..	1	3	2	–	6

Local Authorities		*Eur.*	*Non-Eur.*
Transvaal:			
Nil			
Cape Province:			
Bonnievale Municipality	U		1
Burgersdorp Municipality ..	U		1
Cape Town Municipality ..	U		1
Humansdorp Municipality ..	U		1
Stellenbosch Divisional Council	R		1
Orange Free State:			
Nil			
Natal:			
Pietermaritzburg Borough	U	1	

U = Urban. R = Rural.

* * *

Westdene Products (Pty.) Ltd., 23 Essanby House, 175 Jeppe Street, Johannesburg will be pleased to lend, free of charge, medical sound films, 16 mm., to interested doctors and professional groups. Telephone 23-0314.

NEW PREPARATIONS AND APPLIANCES : NUWE PREPARATE EN TOESTELLE

DISTAQUAINE V-K TABLETS

British Drug Houses announce the arrival of Distaquaine V-K tablets and supply the following information. Distaquaine V-K tablets are a chemically improved form of Distaquaine V tablets. They consist of the potassium salt of penicillin V and are initially being presented in one strength only, each tablet containing the equivalent of 125 mg. of penicillin V free acid.

Distaquaine V-K has been introduced on account of a demand for a product of greater solubility than the free acid preparations (the Distaquaine V series). This requirement is satisfied by the potassium salt of phenoxymethylpenicillin which, because of its faster absorption, will produce earlier peak blood levels and higher therapeutic concentrations, provided that it is administered to the patient in a fasting condition. However, clinical evidence has shown that there is no material increase in therapeutic efficiency over the free acid products. Since their introduction into the Union in 1956, the original free acid preparations (the Distaquaine V range) have given remarkably consistent results and have the great advantage of producing reliable blood levels whether administered to a patient fasting or when given after meals.

The official product included in the British Pharmacopoeia of 1958 will be the free acid (phenoxymethylpenicillin, Distaquaine V) and this taken in conjunction with its proven value and efficiency means that the Distaquaine V range will be continued. Both Distaquaine V-K tablets and Distaquaine V will be available in future, and those doctors who require the earlier somewhat higher blood levels of the potassium salt in fasting patients, will then have a choice of product dependent upon the stage of infection to be treated.

From 14 April 1958 Distaquaine V-K may be prescribed from the following packs: Distaquaine V-K Tablets 125 mg., cartons of 12, bottles of 100 and bottles of 500.

TRILAFON INJECTION (SCHERING CORPORATION, USA)

Scherag (Pty.) Ltd. introduce Trilafon Injection and supply the following information:

Each c.c. of Trilafon Injection contains 5 mg. of perphenazine, an extremely potent tranquillizing and antiemetic drug, in an aqueous vehicle for intramuscular or intravenous injection.

Advantages. Trilafon provides a favourable therapeutic ratio. It has a parenteral milligram potency much greater than other phenothiazine compounds without a corresponding increase in autonomic, hematologic or hepatic side-effects. Smaller doses are therefore required both in patients under treatment with older drugs and in those not previously treated. The degree of adrenergic blockade with Trilafon Injection is considerably less than may be encountered with certain other phenothiazine tranquillizers. Thus significant hypotension has rarely been reported. Deep intramuscular injection is extremely well tolerated; no local reactions, including pain at the site of injection, have been reported. Neither agranulocytosis nor jaundice has been reported.

Indications. Trilafon Injection is indicated as initial therapy or in the treatment of acute episodes in agitated mental and emotional disturbances, acute alcoholism, nausea and vomiting due to various causes, obstetrics, hiccups, chronic pain, and severe pruritus. The tranquillizing and antiemetic effects of Trilafon Injection are also valuable in surgery.

Intramuscular dosage should be individualized and adjusted according to the conditions treated, severity of symptoms, and patient's response. Paediatric dosage has not yet been established; children over 12 may receive the lowest limit of adult dosage. The usual initial dose is 5 mg. (1 c.c.). This may be repeated every 6 hours. The total daily dosage ordinarily should not exceed 15 mg. in ambulatory patients or 30 mg. in hospitalized patients. When required to achieve satisfactory control of symptoms in severe conditions an initial 10 mg. intramuscular dose may be given. The injection should be given with the patient seated or recumbent and the patient should be observed for a short period after administration. Dizziness or significant hypotension after Trilafon Injection is a rare occurrence. Deep intramuscular injection is extremely well tolerated; no local reactions have been reported. Therapeutic effect is usually evidenced in 10 minutes and is maximal in 1-2 hours. The average duration of effective action is 6 hours, and occasionally 12 to 24 hours.

Patients should be placed on oral therapy as soon as practicable. Generally, this may be achieved within 24 hours. However, in some instances, patients have been maintained on injectible therapy for several months. It has been established that Trilafon Injection is more potent than tablets; therefore, equal or higher dosage should be used when the patient is transferred to oral therapy.

Intravenous administration of Trilafon Injection is not recommended except when absolutely necessary to control severe vomiting, intractable hiccups, or acute symptoms such as violent retching during surgery. This route of administration should be used with particular caution and care, and should be limited to recumbent hospitalized adults and to doses not exceeding 5 mg. Employed in this manner, intravenous injection should ordinarily be given as a diluted solution, used either as fractional injection or a slow drip infusion.

Packing. Trilafon Injection, 5 mg. boxes of 6 ampoules. Scherag (Pty.) Ltd., Johannesburg.

REVIEWS OF BOOKS : BOEKRESENSIES

YEAR BOOK OF NEUROLOGY, PSYCHIATRY AND NEUROSURGERY

The Year Book of Neurology, Psychiatry and Neurosurgery. (1956-1957 Year Book Series). Edited by Roland P. Mackay, M.D., S. Bernard Wortis, M.D. and Oscar Sugar, M.D. Pp. 596. $7·00. Chicago: Year Book Publishers, Inc. 1957.

Contents: Neurology—Introduction. Anatomy. Physiology. Pathology. Infectious Diseases. Vascular Disturbances. Degenerative Diseases. Metabolic Disorders. Trauma. Convulsive Disorders. Exogenous Toxins. Neuropathies. Diagnostic and Therapeutic Methods. *Psychiatry*—Introduction. General Topics. Psychodynamic and Psychopathologic Studies. Psychophysiologic Studies. Experimental Psychiatry. Psychosocial Studies. Child Psychiatry. Mental Deficiency. Organic Disorders, Acute and Chronic. Paroxysmal Convulsive Disorders. Schizophrenia and Affective Disorders. Psychoneuroses and Psychosomatic Disorders. Miscellaneous Clinical Syndromes. Military Neuropsychiatry. Therapy. *Neurosurgery*—Introduction. Basic Sciences. Diagnostic Technics. Congenital and Perinatal Disorders. Infections. Trauma. Intracranial Vascular Disease. Brain Tumors. Hypothermia and Hypertension. The Sympathetic Nervous System. Treatment of Pain. Trigeminal Neuralgia. Peripheral Nerves. Convulsive Disorders. Surgery of Involuntary Movements. Miscellaneous.

In this compilation the authors have included abstracts of publications of neurological and psychiatric interest received between November 1955 and October 1956. Most aspects of these fields are represented, though some only briefly, e.g. Psycho-analysis. The material abstracted is largely from American journals, but contributions from farther afield, including our own, make their appearance.

Each section is preceded by an informative introduction reviewing the trends that have emerged during the year under discussion and critically appraising some of the newer developments. A useful list of publications in the field of psychopharmacology occupies an important position in the introduction to the section on psychiatry as does a reference to articles too complicated to abstract and a list of recent interesting psychiatric publications.

With its well organised content and adequate index, this publication is a useful book for the specialist. The neuro-surgical section of this Year Book is edited by Oscar Sugar, M.D. who follows Dr. Percival Bailey who had been editing this section for many years previously.

This section includes abstracts of publications from neuro-surgical, general surgical, medical, radiological, dermatological and anaesthetic journals, from the Americas, Britain, the Continent, Scandinavia and Australia.

There are representative articles on the basic sciences with reference to experimental ultrasonic lesions in animals, and diagnostic techniques with reports of a large variety of new compounds for angiography. Congenital and peri-natal disorders, infections, trauma, vascular disease and brain tumours, are all dealt with. There are a number of abstracts on hypo-thermia and hypotension. The sympathetic nervous system, treatment of pain

and trigeminal neuralgia, also have their representative articles. There are abstracts on the convulsive disorders and the surgery of involuntary movements, and in the final section under 'Miscellaneous', a technique for hypophysectomy and an article on pre-frontal leucotomy are included.

Every neuro-surgeon looks forward to this annual publication and once again, this particular one is not a disappointment.

F.F. and H.M.

ANATOMIES OF PAIN

Anatomies of Pain. By K. D. Keele, M.D., F.R.C.P. Pp. x + 206. Plates XIII, Figs. 14. 27s. 6d. net. Oxford: Blackwell Scientific Publications. 1957.

Contents: Preface. 1. The Sensory Heart. 2. The Greek Debate on the Heart, Brain and Pain. 3. The Central Nervous System Emerges as The Basis of Sensation. 4. The Search for the Sensorium Commune. 5. The Discovery of the Spino-Thalamic Tract. 6. Twentieth-Century Pain Mechanisms. 7. The Structure of Pain. Index.

This work gives an interesting and well documented account of views concerning sensation and, more particularly, pain from the earliest known to the present time. It tells how sensation was first attributed to the heart, thereafter to nerves which, however, proceeded to the heart, in the blood of which was situated the Soul. The work of certain Greek philosophers slowly changed this, but at the time of Galen the contemporary Christian Father Tertullian evoked the testimony of the Gospels to support the older view of Aristotle and others. In time the Latin scholar Albertus Magnus, later canonized, exerted his influence to return to the concept of sensation in the brain. The battle was not yet over, and even great physiologists like Harvey chose Aristotle's view. The story unfolds to the dissections of Charles Bell, the experiments of Magendie and thereafter the evolution of modern concepts on sensation and pain.

The work is of supreme interest to the medical historians and to all interested in neurology and should prove of interest to all other doctors as a well-written and comprehensive survey of a most important subject.

F.E.

CLINICAL EXAMINATION OF THE PATIENT WITH ORGANIC CEREBRAL DISEASE

The Clinical Examination of Patients with Organic Cerebral Disease. By R. Klein, M.D., and W. Mayer-Gross, M.D., F.R.C.P. Pp. xiii+96. Figures 9. 15s. London: Cassel & Co., Ltd. 1957.

Contents: Foreword. Introduction. I. Aphasia. 1. Disturbance of the Motor Act of Speech. 2. Disturbance in Speech Formulation. 3. Defects in Naming (Nominal Aphasia). 4. Disturbance of Speech Comprehension (Word Deafness). 5. Automatic Speech in Aphasia. 6. Defects of Written Language. 7. General Remarks on Aphasia. 8. Musical Disturbances (Amusia) and Disturbances of Rhythm. II. Disorders in the Visual Sphere. 1. Visual-motor Disturbances. 2. Metamorphoptic and Kindred Disorbers. 3. Visual Agnosia. 4. Visual Alexia (Pure Word Blindness). 5. Colour Agnosia. 6. General Remarks on Visual Agnosias. 7. Disturbance in Orientation of the Outside Space. 8. General Remarks on Spatial Disorder. III. Temporal Disorder. IV. Disorders of Motor Actions at a Higher Level. 1. Lack of Motor Impulses and their Excess. 2. Dyspractic Disorders. 3. Disturbance in Special Manual Skills such as Writing, Drawing and Construction (Constructional Disorder). 4. General Remarks on Disturbance of Motor Action of Higher Order. V. Tactile Agnosia. VI. Disturbance Connected with the Body Scheme. 1. Disturbance of the Body Space. 2. Disturbance in Apperception (unawareness) of body parts and of their functions. VII. Disturbance in the Use of Numbers (Acalculia). VIII. Rules of Dominance. IX. General Disturbances. 1. Disturbance of Attention. 2. Disturbance of Intelligence and Thinking. 3. Defects of Memory and Retention. 4. Disturbances of Emotion, Affect and Mood. 5. Disturbance of Consciousness. References. Index.

Developments in the fields of neurology and psychiatry in the last two decades have to a large extent settled the old problem of joint specialism in these two major subjects and it is doubtful if to-day anyone has the intellectual stature, the clinical acumen and the energy to be able to lay claim to being both a first-class neurologist and a first-class psychiatrist at one and the same time. This is not to say that there are not many able neuro-psychiatrists who practice their art with considerable skill and to the great benefit of their patients. Be that as it may there can be no doubt but that the neurologist is not completely trained without a good basic knowledge and understanding of psychiatry, in its present-day broadest meaning. Even more so must the psychiatrist be well skilled in neurology for so very many of the patients presenting with psychiatric problems are ill because of organic brain disease. This book is a satisfactory introduction to the clinical examination and understanding of such conditions. It brings together in comparatively small compass the practical information required for investigating these cases. This is, of course, already available in various larger texts and monographs but it requires much searching of the literature and a long time spent in medical libraries to make it available. It will be especially valuable to those psychiatrists, particularly those in mental hospitals, whose neurological training is little more than of the undergraduate level. The chapter headings indicate the topics dealt with, generally in an adequate fashion, and bibliographical references enable the careful enquirer to pursue the subject in greater detail. It can be confidently recommended also to the medical registrar and the good general practitioner who quite correctly seeks to complete his essential knowledge.

S.B.

CHEMOTHERAPY AND THE CENTRAL NERVOUS SYSTEM

Chemotherapy and the Central Nervous System. By Henry McIlwain, Ph.D., D.Sc. Pp. viii+328. 61 Illustrations. 45s. net. London: J. & A. Churchill Ltd. 1957.

Contents: Preface. 1. Chemical Synthesis of Therapeutic Agents. 2. General Depressants. 3. Control of Body Temperature. 4. The Chemotherapeutic System: I. Bodily Distribution and Metabolism of Drugs. 5. The Chemotherapeutic System: II. Actions of Drugs on the Body and on the Disturbing Agent. 6. Infection: I. The First Specific Agents. 7. Infection: II. Metabolic and Biological Anatagonism. 8. Epilepsy and Anticonvulsants. 9. Analgesics. 10. Nervous and Mental Disorders: I. Drugs Mainly Excitant. 11. Nervous and Mental Disorders: II. Drugs Mainly Depressant. 12. The Nature and Results of Chemotherapeutic Trial. Author Index. Subject Index.

The modern training in therapeutics leaves much to be desired and one must regretfully say that all too often the doctor is instructed in the use of drugs almost solely by the multicoloured publications of the advertising experts who so elaborately and expensively, and even sometimes skilfully push the products of the pharmaceutical manufacturers, an industry which has become very big business indeed. While it is true that reputable firms have established reasonable standards of experimental efficacy and therapeutic trial, products are all too often presented to the doctor with exaggerated claims as to their clinical value and too few of us can undertake our own evaluations of their real benefit. One way for the doctor to avoid the impact of skilful psychological suggestion is to equip himself with the basic chemotherapeutic knowledge that will enable him to use reasonable scientific scepticism when he peruses his daily dozen of advertisements. This book deals with the therapy of the nervous system and it describes methods and principles in chemotherapy as a whole; it deals with the production of drugs for special purposes in cases of the various disorders to which this system is subject and there is some mention of practical clinical application. It is the latter topic, however, which fails to provide the completeness of information that had been hoped for and one must look elsewhere for detailed information of the clinical use and value of the many drugs whose chemical, biochemical, and biological aspects are so adequately dealt with in this text. The subject matter is not conducive to a lightness of literary touch and the book is not an easy one to read, but the specialist in psychiatry and neurology and the post-graduate student will find much of great value in it.

B.S.

CORRESPONDENCE : BRIEWERUBRIEK

EMOLUMENTS OF MEDICAL POSTS IN THE PUBLIC SERVICE

To the Editor: I should like to make the following observation on the letter from Dr. J. J. du P. Le Roux,[1] Secretary for Public Health, which was published in the *Journal* of 5 April:

1. From Dr. Le Roux's own figures over half the medical practitioners in the Public Service are earning £1,380 plus cost of living allowance, or less.

2. Although one may reach £1,380 within 2 years one may stay at that grade for a very long time.

3. Furthermore there are very many medical men in provincial and municipal service who are also held at this £1,380 (fixed) grade with little prospect of improvement.

4. Although Dr. Le Roux manages theoretically to raise a salary of £1,740 plus cost of living allowance to a total of £2,471, the few earning this salary still only get £1,740 plus cost of living allowance on which to live. The other theoretical additions cannot be used to pay for one's house, food, education, and similar expenses.

I should like to suggest that the best remedy for the staff shortage would be found by replacing this £1,380 (fixed) grade by a grade with annual increments as follows: £1,380 (plus cost of living allowance) by £60 per annum to £1,800 plus cost of living allowance, so that experience, service and loyalty would receive a fair reward. Other public servants receive annual increments; so in fairness the medical profession also should.

This grading should also apply to the provincial and municipal administrations. Further the vacation-saving bonus should be granted to all full-time medical practitioners, including municipal staff, and preferably length of leave should be standardized in all three services.

I feel that with this change in salary grading much of the present discontent would be removed, and recruitment would improve rapidly; for there would be a fair income guaranteed to the practitioner of several years' service, and/or experience, at a time when his living expenses are high owing to education costs, etc.

Finally, retiring age should be 65 years in all three services, and widows pension fund apply also to all three services.

'£1,380'

10 April 1958

1. Le Roux, J. J. du P. (1958): S. Afr. Med. J., 32, 386

THE TREATMENT OF POISONING WITH ALKYLPHOSPHATE INSECTICIDES

To the Editor: Owing to the large number of fatal cases of poisoning with insecticides belonging to the alkylphosphate group, everything possible should be done to render treatment of such cases more effective than it is at present. With this object in view I wish to draw attention to some promising developments in this field of research. The alkylphosphate insecticides (Parathion (Thiophos), Paraoxon, etc.—belong to the group of drugs and poisons which exert cholinergic effects. It is therefore quite conceivable that atropine which has anti-cholinergic effects, is, to a certain extent, effective as an antidote in cases of poisoning with these insecticides. However, atropine counteracts only the symptoms of these cholinergic poisons, while the cause of the symptoms, namely the blocking of cholinesterase, persists, resulting in prolongation of the symptoms.

In their investigations, Nachmansohn, Wilson and their collaborators have been investigating the possibility of re-activating the cholinesterase blocked by the alkylphosphates. They found nicotine-hydroxamic acid-methiodide and 2-pyridine aldoxime-methiodide most effective.

Recently, Bethe and his co-workers (Arch. exp. Path. Pharmak., Bd. 231, 1957, p. 3) conducted experiments upon anaesthetized guinea-pigs and on the excised frog heart, excised guinea-pig heart, and excised auricle of the rabbit heart in an attempt to find the most effective substance in the re-activation of the cholinesterase blocked by the above alkyl phosphate insecticides. In their experiments they used (1) nicotine-hydroxamic acid-methiodide (NHMI), (2) 2-pyridine-aldoxime-methiodide (PAM), and (3) pyridine-aldoxime. Of these three cholinesterase reactivators, they found PAM most effective. They were employed in 1·0% solutions and were administered intravenously in doses varying from 30·0 to 60·0 mg. per kg.

Using PAM alone, Bethe *et al.* established that PAM decreased the lethal dose of the alkylphosphates to ¼, but left that of physostigmine unchanged. When they combined the use of PAM with atropine and artificial respiration, the guinea-pigs tolerated 160 times the lethal dose of paraoxon and 20 times that of di-isopropyl-fluorophosphate (DFP).

The results of these preliminary experiments strongly indicate that we possess in PAM a most effective re-activator of the cholinesterase inactivated by the alkylphosphate insecticides. Urgent attempts should be made to encourage firms manufacturing pharmaceutical preparations to place this preparation at our disposal as soon as possible for clinical trials, with full directions.

Douw G. Steyn

Department of Pharmacology
Medical Faculty
University of Pretoria
Pretoria

6 February 1958

INCIDENCE OF CYSTICERCOSIS

To the Editor: We have been investigating the incidence of Cysticercosis and other larval Cestode infestations in Southern Africa. During the course of these studies we have found that in certain Bantu tribes the witchdoctors make use of the proglottids of tape worm, which have been dried and powdered, for the treatment of helminthiasis. This practice is related to the occurrence of exceedingly heavy infestations of Cysticercus cellulosae.

Through your journal may we invite practitioners having further information concerning such practices, or having cases of Cysticercosis on record to communicate with us in order that our paper on this topic should be as comprehensive as possible.

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RADIATION HAZARDS?

To the Editor: I would like to draw the attention of the profession to the apparently conflicting statements by Prof. S. F. Oosthuizen, an eminent South African authority on radiation. These statements were both reported in the lay press and to me are absolutely at variance with one another.

On September 1956, in the *Rand Daily Mail*, Professor Oosthuizen said that 'There is strong evidence that the percentage of physically abnormal people in ceratin parts of the world is increasing. The irreparable damage being done by too frequent X-rays on individuals was another serious problem. It was essential that the number of X-rays given to a patient should be reduced to the minimum. Sometimes as many as 12 plates were taken when 2 would be enough. X-rays have become an important adjunct to the diagnosis of disease, but more and more people were exposing themselves to X-ray diagnostic procedure. These should be cut to a minimum'.

In the *Natal Mercury*, 31 March 1958, he is quoted as saying, 'The potential radiation hazard to man has been grossly exaggerated and he pleaded for a more realistic approach by the public'.

'There was insufficient evidence for today's alarm about radiation, a popular topic for non-scientific writers and one which had sometimes eminated from dramatic statements without sufficient factual basis from certain scientific quarters.' He added 'that scientists differed about whether fission and thermonuclear reactions should be prohibited entirely, notwithstanding the fact that the radiation from these sources remain slight'.

He warned that the radiation danger—*magnified out of all proportions*—was already endangering the numbers of vitally needed pupil radiographers. He stated further 'that it was possible that the potential hazard to man of nuclear and other radiations might restrain intending trainees to come forward'.

I feel that these statements call for clarification, especially as the latest one is at variance with the findings of leading scientific workers in this field. Durbach[1] states 'that all stress the danger to man of background radiation and the over enthusiastic and uncontrolled use of radiation in medical practice and in other spheres of life'.

One is certainly seeing cases of over-radiation and one feels that the problem is becoming more serious all the time and will continue to do so.

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1. Durbach, D. (1957): S. Afr. Med. J., 31, 187.